RELATIVE BIOLOGICAL EFFECTIVENESS (RBE) FACTORS FOR USE IN CALCULATING PROBABILITY OF CAUSATION OF RADIOGENIC CANCERS

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INTRODUCTION

This report presents relative biological effectiveness (RBE) factors for different types of ionizing radiations for use in calculating the probability of causation of specific cancers in humans. The RBE factors developed in this report are expressed as probability distributions which are intended to represent uncertainties in relevant radiobiological data and other judgments involved in evaluating available information. The ionizing radiations of concern include photons (gamma rays and *X* rays),[2] electrons, alpha particles, and neutrons. Except in cases of exposure of the lung to alpha particles emitted by the short-lived decay products of radon in air, the probability distributions of RBE factors are intended to be applied in calculating the probability of causation of radiogenic cancers in any organ or tissue and for any exposure situation.[3]

The probability distributions of RBE factors developed in this report are intended to represent differences in the biological effectiveness of different radiation types in causing stochastic effects in humans, primarily cancers. RBE factors take into account that, for a given absorbed dose in tissue, the probability of a stochastic response depends on the radiation type, and sometimes its energy, as well as the absorbed dose. For a particular radiation of concern, the probability distribution of the RBE factor represents data on RBE obtained from relevant radiobiological studies. The RBE of radiation i compared with a reference radiation, r, is defined as the absorbed dose of the reference radiation (D_r) required to produce a specific level of response relative to the absorbed dose of the radiation of concern (D_i) required to produce an equal response:

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[2]Gamma rays are electromagnetic radiations emitted in de-excitation of atomic nuclei, whereas *X* rays are electromagnetic radiations emitted in de-excitation of atomic electrons, referred to as characteristic *X* rays, or electromagnetic radiations produced in deceleration of charged particles (e.g., electrons) in passing through matter, referred to as continuous *X* rays or bremsstrahlung.

[3]The probability of causation of lung cancer due to inhalation of radon and its short-lived decay products is calculated based on an estimate of the risk per unit exposure to the short-lived alpha-emitting decay products in Working Level Months (WLM), and an RBE factor for alpha particles that would be applied to estimates of absorbed dose in the lung is not used.

$$\mathrm{RBE}_i = \frac{D_r}{D_i}, \quad (1)$$

with all physical and biological variables, except differences in radiation type, being held as constant as possible. Values of RBE are specific to each study, and they generally depend on the biological system and specific response under study, the magnitude of the absorbed doses, the dose rate, and the dose per fraction if the dose is fractionated.[4]

In most radiobiological studies in which RBEs were estimated, the reference radiation was either orthovoltage *X* rays (usually 180-250 kVp)[5] or higher-energy gamma rays produced in the decay of ^{60}Co (photon energies of 1.2 and 1.3 MeV) or, less frequently, ^{137}Cs (0.66 MeV). Knowledge of the reference radiation in any study is important because, as discussed in this report, the biological effectiveness of *X* rays apparently is greater than that of higher-energy gamma rays. In this report, the reference radiation is taken to be high-energy gamma rays, specifically the gamma rays emitted in ^{60}Co decay. This choice is appropriate for the purpose of developing RBE factors for use in calculating the probability of causation of cancers because estimates of cancer risks in humans are based primarily on data obtained from studies of the Japanese atomic-bomb survivors who were exposed mainly to high-energy gamma rays.[6]

The probability distributions of RBE factors in humans presented in this report are based primarily on published reviews and evaluations of radiobiological studies. For the most part, we relied on reviews by such expert groups as the International Commission on Radiological Protection (ICRP), the International Commission on Radiation Units and Measurements (ICRU), the National Council on Radiation Protection and Measurements (NCRP), the U.K.'s National Radiological Protection Board (NRPB), and the Committee on Interagency Radiation Research and Policy Coordination (CIRRPC), as well as reviews by individuals who are recognized experts. We used other information from the primary literature only to a limited extent.

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[4]Although the term "RBE factor" is used in this report to describe the biological effectiveness of different radiations in inducing cancers in humans, we recognize that these factors are not true RBEs. In accordance with the definition given above, the term "RBE" strictly applies only to the results of specific radiobiological studies, but RBE factors in humans generally are assumed values that are based on evaluations of studies in other biological systems.

[5]The term "kVp" denotes the maximum potential difference in kilovolts (kV) across an *X*-ray tube during an exposure; this potential difference determines the maximum electron energy in keV. The average energy of the continuous spectrum of bremsstrahlung produced when the electrons are stopped in a target is a small fraction of the peak tube potential in kVp.

[6]At the present time, the only cancer risks that are not estimated based on data in the Japanese atomic-bomb survivors, in addition to the risks of lung cancer from inhalation of radon and its short-lived decay products, are the risks of thyroid cancer resulting from exposure in childhood (Land et al., 2002). These risks are estimated based primarily on studies of children who were exposed to *X* rays.

The probability distributions of RBE factors developed in this report are intended to represent uncertainties in values that should be used to calculate the probability of causation of radiogenic cancers. It cannot be overemphasized that the development of these probability distributions relies to a significant extent on subjective scientific judgment. The most important judgment is an assumption that RBEs obtained from studies of a number of stochastic responses in a variety of biological systems are applicable to induction of cancers in humans. This assumption is necessitated by the lack of data on RBEs for cancer induction in humans. Scientific judgment also is applied by experts and expert groups in their reviews and evaluations of published studies, and in the conclusions they draw from these reviews. Finally, we have applied our own scientific judgments in developing probability distributions of RBE factors, and we recognize that knowledgeable individuals could reach somewhat different conclusions based on the same body of information.

In this report, we have assumed that the probability distributions of RBE factors apply to all cancers. We have not explicitly taken into account the possibility that the biological effectiveness of some radiations may depend on the particular cancer of concern. For example, in some studies of neutrons and alpha particles, RBEs for leukemias and lymphomas appear to be less than RBEs for solid tumors (NCRP, 1990; Muirhead et al., 1993; EPA, 1994; Edwards, 1997; Edwards, 1999). We have accounted for such differences only in a general way by developing probability distributions of RBE factors that are sufficiently broad to encompass available data for all stochastic responses studied.

In developing probability distributions of RBE factors for use in calculating the probability of causation of radiogenic cancers, an important consideration is the extent to which these distributions should be consistent with recommendations developed by national and international advisory groups for purposes of radiation protection. In radiation protection, the quantities that are analogous to an RBE factor are the effective quality factor, $\overline{Q}$ (ICRU, 1986), and the radiation weighting factor, w_R (ICRP, 1991; NCRP, 1993).[7]

Effective quality factors and radiation weighting factors used in radiation protection are prescribed point values that are intended to represent relevant data on RBE. For the radiation types considered in this report, the values of $\overline{Q}$ recommended by the ICRU (1986), which were developed by a Joint Task Group of the ICRP and the ICRU, and the values of w_R currently recommended by the ICRP (1991) and the NCRP (1993) are given in Table 1. Although there is general agreement between the two sets of recommendations, there are some differences, especially in the recommendations for photons of energy less than 30 keV and low-energy beta particles emitted in the decay of tritium (^{3}H). There also are smaller differences in the recommendations for alpha particles and neutrons.

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[7]The effective quality factor is intended to be applied to the radiations at the locations in tissue where an absorbed dose is delivered, whereas the radiation weighting factor is intended to be applied to the radiations incident on the body or the radiations emitted by internally deposited radionuclides.

Although consistency between the RBE factors developed in this report and the effective quality factors and radiation weighting factors recommended by national and international authorities may be desirable, there are two important factors to be considered. First, point estimates of radiation protection quantities do not reveal the state of knowledge (uncertainty) in these values, including uncertainties in the RBEs obtained from relevant radiobiological studies and uncertainties in other judgments used to develop the point estimates. A full accounting of uncertainties in all parameters is essential when estimating probability of causation for the purpose of evaluating claims by individuals that their cancer was caused by radiation exposure.

Second, for some radiations, it is evident that the recommended point values of radiation protection quantities given in Table 1 are not consistent with the preponderance of relevant radiobiological information. For example, the ICRU (1986) concluded that there is clear evidence that the biological effectiveness of orthovoltage *X* rays and other photons of energy less than about 0.2 MeV is about twice that of high-energy ^{60}Co gamma rays. This conclusion was based on a review of data on RBEs for orthovoltage *X* rays and a calculation of the energy dependence of the effective quality factor for photons shown in Fig. 1. Nonetheless, neither the ICRU nor the ICRP and the NCRP have incorporated this difference in their recommendations on radiation protection. Similarly, the ICRP and the NCRP have not taken into account the clear evidence from available data and a calculation by the ICRU (1986) that beta particles emitted in decay of ^{3}H are biologically more effective than higher-energy electrons and photons.

It is important to recognize that the needs of radiation risk assessment and calculations of probability of causation in cases where actual exposures of specific individuals are of concern differ significantly from the needs of radiation protection. The primary concern in radiation protection is control of exposures based on evaluations of compliance with applicable limits on radiation dose and other radiation protection requirements, but without undue concern for actual doses and risks to exposed individuals and their uncertainties. The use of standard and simplified assumptions for this purpose is appropriate. However, as noted above, estimates of probability of causation must be based on the state of knowledge of actual doses and risks to exposed individuals. Thus, although we have relied on reviews and evaluations of available radiobiological data by such groups as the ICRU, the ICRP, and the NCRP, we have not assumed *a priori* that the effective quality factors or radiation weighting factors given in Table 1 provide "best" estimates of RBE factors for use in calculating probability of causation. As discussed in the following sections, the probability distributions of RBE factors for neutrons and alpha particles developed in this report encompass the recommended values of radiation protection quantities in Table 1, but the probability distributions of RBE factors for lower-energy photons and electrons depart substantially from the recommendations of the ICRP and the NCRP.

The following sections present the probability distributions of RBE factors for neutrons, alpha particles, photons, and electrons. Neutrons are discussed first because they have been the most studied and alternative approaches to estimating RBEs have been developed. An understanding of these approaches is useful in developing RBE factors for the other radiations.

RBE FACTORS FOR NEUTRONS

Approaches to Estimating RBEs

RBEs for neutrons have been estimated in many studies involving different organisms, stochastic endpoints (responses), and doses and dose rates. Most studies used fission neutrons or other neutrons of comparable energies; relatively few studies used neutrons of lower or higher energies. Extensive reviews and evaluations of these data have been presented by the ICRU (1986), the NCRP (1990), and the NRPB (Edwards, 1997).

In most studies, the doses and dose rates of neutrons and the reference radiations were substantially above levels that are encountered in routine exposures of workers and the public. Furthermore, as illustrated in Fig. 3, RBEs for neutrons generally increase with decreasing dose. Therefore, an important focus of radiobiological studies and reviews by expert groups has been to develop estimates of RBE that are appropriate at low doses and dose rates. These RBEs are obtained by extrapolation of data on dose-response for neutrons and the reference radiation at higher doses and dose rates. An RBE at low doses and dose rates obtained by this extrapolation usually is denoted by RBE_M. Summaries of estimated values of RBE_M for fission neutrons developed by the ICRU (1986) and the NCRP (1990) are given in Table 2.[8]

From an evaluation of values of RBE_M obtained from different studies that are deemed relevant to estimating cancer risks in humans, a representative RBE factor at low doses and low dose rates, denoted by $\overline{RBE}_M$ in this report, is chosen.[9] This estimate is a point value for purposes of radiation protection (e.g., a radiation weighting factor, w_R), but is expressed as a probability (uncertainty) distribution for purposes of estimating cancer risks and probability of causation in cases of exposure of specific individuals. Using the RBE at low doses and low dose rates, the cancer risk per unit absorbed dose, R, at low doses and dose rates can be estimated as

$$R = \overline{RBE}_M \times \frac{R_{\gamma,H}}{DDREF_\gamma} , \qquad (2)$$

where $R_{\gamma,H}$ is the cancer risk per unit absorbed dose at high doses and high dose rates of gamma rays (e.g., the excess relative risk, ERR, per Gy, as estimated mainly from studies of the Japanese

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[8]In some cases including, for example, the evaluation of data on tumor induction by the NCRP (1990), values of RBE_M obtained in some studies lie outside the range given in Table 2. Furthermore, the ranges in Table 2 generally are based on central estimates of RBE_M, and values outside these ranges cannot be ruled out when uncertainties in the estimates are taken into account.

[9]We denote an assumed RBE factor for induction of cancers in humans by $\overline{RBE}$ to distinguish this quantity from an RBE obtained from a specific study in a particular biological system and to indicate that an RBE factor is intended to represent a variety of RBEs obtained from different studies.

atomic-bomb survivors) and $DDREF_\gamma$ is the dose and dose-rate effectiveness factor, which takes into account that cancer risks per unit dose at low doses and low dose rates of gamma rays (and other low-LET radiations) may be less than risks per unit dose at high doses and high dose rates in study populations. For example, for purposes of radiation protection, the ICRP (1991) and the NCRP (1993) currently recommend a $DDREF_\gamma$ of 2; i.e., estimated cancer risks per unit dose in the atomic-bomb survivors are reduced by a factor of 2 in estimating risks from exposure to gamma rays and other low-LET radiations at lower doses and dose rates. As indicated by the summary in Table 2, the values of RBE_M for fission neutrons obtained from different studies vary widely. Thus, a probability distribution of $\overline{RBE}_M$ that would represent these data for purposes of calculating probability of causation would span a wide range of values.

In most studies, the dose-response relationship for neutrons is linear at absorbed doses of a few Gy or less, whereas the dose-response relationship for the low-LET reference radiation is linear-quadratic in form (ICRU, 1986; NCRP, 1990); see Fig. 4. Thus, the variability in values of RBE_M for neutrons obtained from different studies is due in part to pronounced differences in the linear-quadratic dose-response relationships for the reference radiations, which result in a wide range of DDREFs for these radiations when calculated as shown in Fig. 5 (CIRRPC, 1995; Edwards, 1997; Edwards, 1999). That is, RBE_M is sensitive to variations in the biological effectiveness at low doses of the reference radiations, with higher values of RBE_M associated with high DDREFs and lower values with low DDREFs. Since the DDREFs for the reference radiations embodied in the values of RBE_M for neutrons generally are not the same as the value of $DDREF_\gamma$ that might be used to adjust observed cancer risks in humans at high doses and high dose rates of gamma rays to obtain estimates of risk at low doses and low dose rates, a probability distribution of $\overline{RBE}_M$ that is based on the variability in estimates of RBE_M may not provide the best representation of the biological effectiveness of low doses of neutrons in humans relative to low doses and dose rates of gamma rays.

For the purpose of estimating probability of causation of cancers at low doses and dose rates of neutrons, difficulties with developing a representative probability distribution of $\overline{RBE}_M$ based on estimates of RBE_M obtained from different studies can be addressed by using an alternative approach recommended by CIRRPC (1995) and discussed by Edwards (1997; 1999). This approach is based on an assumption that RBE factors for neutrons in humans should be consistent with the data used to estimate cancer risks from exposure to photons. That is, the appropriate RBE factors are values obtained from studies in which the reference radiations were gamma rays at high doses and high dose rates, because this was the condition of exposure of the Japanese atomic-bomb survivors from which most estimates of cancer risks in humans have been derived. Thus, if the DDREF for neutrons is assumed to be unity, based on the observation that the dose-response relationship usually is linear at absorbed doses of a few Gy or less and the usual presumption of linearity at low doses for all high-LET radiations, the risk per unit absorbed dose from exposure to neutrons at low doses and low dose rates can be estimated as

$$R = \overline{RBE}_H \times R_{\gamma,H} , \qquad (3)$$

where $\overline{RBE}_H$ is the probability distribution of the RBE factor that represents data on RBE for neutrons at high acute doses of the reference radiation and $R_{\gamma,H}$ again is the risk per unit absorbed dose at high doses and high dose rates of gamma rays. In this approach, the cancer risk does not depend on the value of $DDREF_\gamma$ in humans. Since the DDREF for neutrons is assumed to be unity, eq. (3) also applies at high doses and high dose rates of neutrons.

When the approach in eq. (3) is used to estimate risk, there still is considerable variability in estimates of RBE for neutrons at high acute doses of the reference radiations, RBE_H. This variability is due to several factors including the variety of biological systems and stochastic endpoints studied, as well as the dependence of RBE on dose (see Figs. 3 and 4). However, the variability in RBE_H is considerably less than the variability in RBE_M, due mainly to the reduced influence at high doses of differences in the DDREFs for the reference radiations. Therefore, the uncertainty in a representative value of $\overline{RBE}_H$ should be less than the uncertainty in $\overline{RBE}_M$.

It is important to emphasize that estimates of cancer risks at low doses and dose rates of neutrons obtained using eq. (3) would be the same as risks estimated using eq. (2) if the values of DDREF for the reference radiations embodied in the values of RBE_M were the same as the value of $DDREF_\gamma$ that is used to adjust observed risks at high doses and high dose rates of gamma rays in humans to obtain estimates of risk at low doses and low dose rates. The advantage of using the approach in eq. (3) is that it is directly compatible with the data in the Japanese atomic-bomb survivors who were exposed at high doses and high dose rates. Again, these are the data from which most estimates of cancer risks in humans are obtained.

RBE Factor for Fission Neutrons

Based on the discussion of alternative approaches to estimating RBEs for neutrons, we develop a probability distribution of $\overline{RBE}_H$ for fission neutrons to be used in estimating cancer risks at any dose and dose rate in accordance with eq. (3). This probability distribution is developed based on the results of an analysis of RBEs at high acute doses of the reference radiations by Edwards (1999); see also a report of the NRPB (Edwards, 1997). Values of RBE_H derived by Edwards (1999) from an analysis of data obtained in several studies of life-shortening and induction of specific cancers in mice are summarized in Tables 3-5.[10] Since life-shortening in mice was due mainly to induction of cancers, the different endpoints are closely related. Values of RBE_M derived by Edwards also are given in the tables. In all studies summarized in these tables, the reference radiation was high-energy gamma rays.

The data in Tables 3-5 illustrate two points discussed previously. First, RBEs at high doses and dose rates generally are less than the corresponding extrapolated values at low doses and dose rates, due primarily to the influence of the DDREF for the reference radiation on the

[10]Values of RBE_H given by the NRPB (Edwards, 1997) incorporate an assumed DDREF of 2 for the reference radiations and, thus, are a factor of 2 higher than the values given in the later paper by Edwards (1999). The values in Edwards (1999) are the appropriate ones for use in eq. (3).

extrapolated values. Second, the variability in RBE_H is less than the variability in RBE_M, due primarily to the reduced influence of differences in the DDREFs for the reference radiations in the various studies. For example, in the studies summarized in Tables 3 and 4, the DDREF for the reference radiation, as estimated by the ratio of the mean value of RBE_M to the mean value of RBE_H, varies from 1 to nearly 20.

Life-shortening and induction of specific cancers in mice should be especially relevant to estimating RBE factors for cancers in humans. Therefore, based on the estimates of RBE_H and their standard errors summarized in Tables 3-5, we describe the RBE factor, $\overline{RBE}_H$, for fission neutrons to be used in eq. (3) by a lognormal probability distribution having a 95% confidence interval between 1.5 and 30. This distribution has a geometric mean and geometric standard deviation of 6.7 and 2.2, respectively, and an arithmetic mean of 9.0. A lognormal probability distribution was selected based mainly on the variability in the estimates of RBE_H and the difficulty in judging a credible upper bound of possible values. Truncation of the lower tail of the distribution at 1.0, based on an assumption that the biological effectiveness of neutrons should not be less than that of high-energy gamma rays, is discussed later in this section. The assumed probability distribution of $\overline{RBE}_H$ for fission neutrons applies to a spectrum of energies that ranges from 0.1-15 MeV; this spectrum has a most probable energy of 0.8 MeV and an average energy of 2.0 MeV (Shleien et al., 1998).

Data obtained from studies of tumor induction in other animals are consistent with the probability distribution of $\overline{RBE}_H$ for fission neutrons described above. For example, Wolf et al. (2000) deduced an RBE of about 20-25 for induction of lethal tumors in Sprague-Dawley rats at an acute dose of fission neutrons of 0.1 Gy. In a study in which monkeys were given average doses of 6.7 Gy of *X* rays and 3.4 Gy of fission neutrons, Broerse et al. (1991) derived an RBE for tumor induction of about 4-5. When this value is adjusted to account for the difference of about a factor of 2 in the biological effectiveness of *X* rays and gamma rays, as discussed in a later section, an RBE relative to gamma rays of about 8-10 is obtained. Other studies of tumor induction in animals are discussed by the NCRP (1990).

The probability distribution of $\overline{RBE}_H$ for fission neutrons can be compared with the effective quality factor, $\overline{Q}$, for neutrons of unknown energy recommended by the ICRU (1986) and the radiation weighting factor, w_R, for neutrons of energy 0.1-2 MeV recommended by the ICRP (1991) and the NCRP (1993); see Table 1. The point values of $\overline{Q}$ and w_R are based on estimates of RBE_M and, thus, would be used to estimate cancer risks in accordance with eq. (2). If we assume a $DDREF_\gamma$ of 2 as normally used in radiation protection (ICRP, 1991; NCRP, 1993), the probability distribution of $\overline{RBE}_H$ would correspond to a distribution of $\overline{RBE}_M$ having a 95% confidence interval between 3 and 60.[11] Therefore, the probability distribution of $\overline{RBE}_H$

[11]This confidence interval does not represent the range of values of RBE_M for fission neutrons obtained from analyses of different radiobiological studies, because DDREF for the reference radiation often differed greatly from the value of 2 assumed here. As illustrated in Tables 3-5, upper confidence limits of RBE_M considerably greater than 60 are obtained in some studies (see also Table 2).

for fission neutrons, when multiplied by a $DDREF_\gamma$ of 2, encompasses the point values of quantities that have been recommended for use in radiation protection.[12]

Consideration of Cancer-Specific RBEs

The probability distribution of $\overline{RBE}_H$ for fission neutrons described above is intended to be applied to all cancers in humans. However, some studies in animals suggest that RBEs for leukemias and lymphomas are less than RBEs for solid tumors (NCRP, 1990; Edwards, 1997; Edwards, 1999). Such a difference is indicated, for example, by estimates of RBE_H and RBE_M for specific cancers in RF/Un and RFM mice given in Table 4.

In this report, we have not developed separate probability distributions of RBE factors for leukemias or lymphomas and solid tumors, mainly because a significant difference in RBEs is not shown in all studies. For example, RBEs for myeloid leukemia in CBA/H mice given in Table 4 are about the same as RBEs for solid tumors in BALB/c and SAS/4 mice. Furthermore, the central estimates of RBE_H from all studies given in Table 4 suggest that the difference in RBEs for leukemias and solid tumors is no more than about a factor of 2. Similarly, the results of a study using B6CF1 mice given in Table 5 do not show a significant difference in RBEs for lymphocytic tumors and other tumors. We have accounted for possible cancer-specific differences in RBEs for fission neutrons only in a general way by defining the probability distribution of $\overline{RBE}_H$ so that the 95% confidence interval encompasses the full range of estimates of RBE_H and their uncertainties given in Tables 3-5.

RBE Factors at Other Energies

Estimation of cancer risks in humans from exposure to neutrons is complicated by the apparent dependence of RBEs on neutron energy. This energy dependence is represented by the radiation weighting factors currently recommended by the ICRP (1991) and the NCRP (1993) for use in radiation protection (see Table 1 and Fig. 6). In comparison, the quality factors at different neutron energies currently used by the U.S. Nuclear Regulatory Commission (NRC, 1991) and the U.S. Department of Energy (DOE, 1993) are given in Table 6. These quality factors were developed by the NCRP (1971) based on calculated depth-dose distributions in a cylindrical phantom or tissue slab at incident neutron energies of 0.025 eV to 400 MeV. The recommended radiation weighting factors and the quality factors used by regulatory authorities indicate that the probability distribution of $\overline{RBE}_H$ for fission neutrons described above applies at energies that have the highest biological effectiveness.

The reductions in the radiation weighting factor at neutron energies outside the range of 0.1-2 MeV recommended by the ICRP (1991) and the NCRP (1993) are based mainly on limited

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[12]The point values of $w_R = 20$ and $\overline{Q} = 25$ in Table 1 are at about the 70th and 80th percentiles, respectively, of this probability distribution.

data obtained from studies in animals and cell cultures, which are reviewed by the NCRP (1990) and the NRPB (Edwards, 1997), and calculations of the quality factor vs. neutron energy, such as those given in Fig. 2 (ICRU, 1986) and Table 6 (NCRP, 1971). Other studies of the energy dependence of the biological effectiveness of neutrons are discussed by the NCRP (1990) and Edwards (1997). The ICRP (1991) also suggested that its recommended step function for the radiation weighting factor given in Table 1 can be represented by a smooth function of the form

$$w_R = 5 + 17\exp[-(\ln(2E))^2/6] \ , \qquad (4)$$

where E is the neutron energy in MeV. This relationship is not intended to imply any biological significance, but it does provide a convenient calculational tool when incident neutron energies are well known. The smooth function in eq. (4) is compared with the recommended step function for the radiation weighting factor in Fig. 6.

We define the energy dependence of the RBE factor for neutrons, $\overline{\mathrm{RBE}}_H$, to be used in eq. (3) in the following way. In the ICRP's step-function representation of w_R given in Table 1 and Fig. 6, the values at energies other than 0.1-2 MeV are a factor of 2 or 4 less than the value that applies to fission neutrons. Thus, as a first approximation, when neutron energies are outside the range of 0.1-2 MeV, the probability distribution of $\overline{\mathrm{RBE}}_H$ for fission neutrons could be reduced by a factor of 2 or 4, depending on the energy. For example, a reduction by a factor of 2 would apply to 14-MeV neutrons produced by the ^{3}H(d,n)^{4}He reaction at low projectile energies, and a reduction by a factor of 4 would apply to thermal neutrons.

However, uncertainties in the energy-dependent reduction factors also should be taken into account. Based on data shown in Figs. 7 and 8 and other data reviewed by the NRPB (Edwards, 1997) and the NCRP (1990), we represent the reduction factor at neutron energies of 10-100 keV or 2-20 MeV by a lognormal probability distribution having a 95% confidence interval between 1.0 and 4.0. This distribution has a geometric mean and geometric standard deviation of 2.0 and 1.4, respectively, and an arithmetic mean of 2.1. Based on calculations by the NCRP (1971) which indicate that the biological effectiveness should decrease as the neutron energy decreases below 10 keV or increases above 20 MeV, we then represent the reduction factor at these energies by a lognormal probability distribution having a 95% confidence interval between 2.0 and 8.0. The geometric and arithmetic means of this distribution are twice the values given above, and the geometric standard deviation is the same.

The probability distributions of the energy-dependent reduction factors described above represent assumptions that the values probably differ from the central estimates of 2 or 4 by no more than a factor of 2, and that values above and below the central estimates are equally likely. However, the assumed distributions also give a small weight to the possibility that the reduction factors differ from the central estimates by more than a factor of 2. For example, the probability distribution of the reduction factor at neutron energies of 10-100 keV gives a weight of 2.5% to an assumption that the RBE factor is somewhat higher than the value at energies of 0.1-2 MeV. This assumption is supported by the data summarized in Fig. 7 and by the results of a study by

Miller et al. (2000) which indicated that the biological effectiveness of 70-keV and 350-keV neutrons was not significantly different. Uncertainties in these reduction factors should be smaller than the uncertainty in $\overline{\text{RBE}}_{\text{H}}$ for fission neutrons.

Correction for Inverse Dose-Rate Effect

An additional consideration in estimating cancer risks from exposure to neutrons is the possibility that the biological effectiveness of neutrons, and other high-LET radiations, increases as the dose rate decreases. This phenomenon is referred to as the inverse dose-rate effect. Some studies of life-shortening and tumor induction in small mammals at relatively high doses of fission neutrons reviewed by the NCRP (1990), the ICRP (1991), and CIRRPC (1995) show an enhancement in biological effectiveness by as much as a factor of about 3 when the same dose is delivered at lower dose rates. However, this effect is not seen in all studies of these endpoints at high doses, and it usually is not seen at lower doses.

Although it is not clear whether the mechanisms responsible for the observed inverse dose-rate effect for fission neutrons in some studies would apply in estimating cancer risks in humans, especially at low doses (CIRRPC, 1995), we apply a small correction factor to account for this effect. This correction, which we refer to as an enhancement factor, is applied only in cases of chronic exposure to neutrons of any energy; it does not apply to acute exposures.

Based on discussions and summaries of data on life-shortening and tumor induction in small mammals given in Sections 6 and 8 and Tables 6.2 and 8.2 of NCRP (1990), we assume a probability distribution for the enhancement factor representing the inverse dose-rate effect under conditions of chronic exposure to neutrons that ranges from 1 to 3 and is weighted toward lower values. Specifically, we assume a discrete probability distribution with 50% of the values at 1.0, 30% at 1.5, 15% at 2.0, and 5% at 3.0. The arithmetic mean of this distribution is 1.4. This distribution takes into account that the effect is not seen in all studies at high doses and usually is not seen at low doses of greatest interest in routine exposures of workers and the public.

Summary

Cancer risks in humans at any dose and dose rate of neutrons are estimated using an approach represented by eq. (3). Specifically, the risk per unit absorbed dose from exposure to neutrons (n) is estimated as

$$R_n = \overline{\text{RBE}}_{n,\text{H}} \times \text{AF}_n \times \text{EF}_n \times R_{\gamma,\text{H}} , \qquad (5)$$

where $\overline{\text{RBE}}_{n,\text{H}}$ is the RBE factor for fission neutrons at high doses and high dose rates of gamma rays, AF_n is an energy-dependent adjustment factor that represents the reduction in biological effectiveness of neutrons when the energy is outside the range of 0.1-2 MeV, EF_n is an enhancement factor that represents the inverse dose-rate effect for chronic exposure to neutrons of any energy, and $R_{\gamma,\text{H}}$ is the risk per unit dose at high doses and high dose rates of gamma rays.

Thus, the biological effectiveness of neutrons relative to high doses and high dose rates of gamma rays is represented by a combination (aggregate) of up to three probability distributions that take into account the different factors of concern and their uncertainties.

Given the assumed probability distributions of each of the factors summarized above, the probability distribution of the RBE factor for neutrons in specific cases will include some values less than 1.0. In all cases, however, the lower tail of the aggregate probability distribution should be truncated at 1.0. This truncation is based on an assumption that, since some of the dose due to incident neutrons of any energy would be delivered by high-LET radiations (NCRP, 1971; ICRP, 1997), the biological effectiveness of neutrons should not be less than that of high-energy gamma rays. The lower tail should be truncated only after the aggregate probability distribution representing the combination of all relevant factors contributing to the RBE factor for a given exposure situation is obtained.

It is possible that the RBE factor for neutrons in humans could be less than 1.0 when most of the dose is delivered by the 2.2-MeV gamma rays emitted following capture of thermalized neutrons by ^{1}H nuclei. This situation could occur when the incident neutron energy is less than about 10 keV (NCRP, 1971). The possibility of an RBE factor less than 1.0 at low energies is based on the consideration that the biological effectiveness of 2.2-MeV gamma rays could be somewhat less than that of the reference ^{60}Co gamma rays used in studies to estimate RBEs (Straume, 1995). However, we do not believe that this difference needs to be taken into account in estimating RBE factors for neutrons. The reduction in the biological effectiveness of 2.2-MeV gamma rays relative to ^{60}Co gamma rays should be less than a factor of 2 (Straume, 1995). This difference should be small compared with possible errors in estimating cancer risks that result from an assumption that the spectrum of photons to which the Japanese atomic-bomb survivors were exposed has the same biological effectiveness as ^{60}Co gamma rays. This assumption is implicit in the RBE factors for neutrons, and other radiations, developed in this report.

It also is possible that the assumed probability distributions of the RBE factors for neutrons could tend to overestimate cancer risks in humans, especially at energies greater than about 0.1 MeV. In studies in small mammals that were used to estimate RBEs for fission neutrons, a substantial fraction of the dose to target tissues was delivered by high-LET radiations (e.g., recoil protons). In humans, however, more of the dose to deep-lying organs and tissues would be delivered by gamma rays produced by neutron interactions in tissue. Therefore, RBEs obtained from studies in small mammals should tend to overestimate the biological effectiveness of incident fission neutrons in most organs and tissues of humans (ICRP, 1997; Edwards, 1997; Edwards, 1999). However, we have not adjusted the RBE factors for neutrons to account for possible differences in biological effectiveness in humans compared with small mammals, mainly because calculations indicate that this difference depends in a complicated way on the neutron energy, the particular target tissue, and the irradiation geometry (ICRP, 1997). We have accounted for such differences only in a general way by defining probability distributions of the RBE factors for neutrons to include values as low as 1.0.

RBE FACTOR FOR ALPHA PARTICLES

Approach to Estimating RBEs

Like neutrons, alpha particles are high-LET radiations that have been shown to be considerably more effective than low-LET radiations in inducing stochastic responses in biological systems. Alpha particles also are presumed to have a linear dose-response relationship at doses below those where significant cell killing occurs. Thus, in principle, it would be desirable to estimate cancer risks in humans exposed to alpha particles based on estimates of RBE at high acute doses of high-energy gamma radiation, RBE_H, in accordance with eq. (3), as we have done for neutrons, to lessen the influence of variations in the DDREF of the reference radiation. The importance of the DDREF of the reference radiation is indicated by the pronounced increase in RBEs with decreasing dose of alpha particles in the studies summarized in Fig. 9. As is the case with neutrons, high estimates of RBEs at low doses, RBE_M, may be due, at least in part, to high values of DDREF for the reference radiation.

As discussed below, however, most studies of alpha particles did not use high acute doses of gamma rays as the reference radiation. Furthermore, an analysis to estimate RBEs for alpha particles at high acute doses of the reference radiation, similar to the analysis for neutrons by Edwards (1997; 1999), has not, to our knowledge, been performed. Such an analysis is not straightforward, due to the dependence of the DDREF of the reference radiation on the chosen value of a high dose (see Fig. 5). Therefore, for alpha particles, we developed a probability distribution of the RBE factor at low doses and dose rates of the reference radiation, $\overline{RBE}_M$, for use in eq. (2). This distribution is based on estimates of RBE_M obtained from various studies.

Alpha particles are somewhat simpler than neutrons in that the range of energies that occur in radioactive decay is limited. A calculation of the energy dependence of the effective quality factor by the ICRU (1986), shown in Fig. 10, indicates that the biological effectiveness of alpha particles is nearly independent of energy over the energy range of concern. We have assumed that a single probability distribution of the RBE factor can be applied to all alpha particles that occur in radioactive decay.

Development of RBE Factor

Data on RBEs for alpha particles emitted in the decay of radionuclides have been reviewed by the NCRP (1990) and the NRPB (Muirhead et al., 1993); see also Sinclair (1996). Compared with neutrons, estimation of RBEs for alpha particles is complicated by the fact that the reference radiation in most studies was not high-energy gamma rays. In some studies in mammalian cell systems, the reference radiation was *X* rays, and in studies of induction of bone or lung tumors in mammals, the reference radiation usually was the continuous spectrum of beta particles emitted in the decays of ^{90}Sr and ^{90}Y or other radionuclides. However, the difference between using electrons from beta decay and high-energy gamma rays as the reference radiation may not be significant, because studies discussed in Section 7.3 of NCRP (1990) indicated that

beta particles from ^{144}Ce decay and protracted ^{60}Co gamma rays are equally effective in producing chromosome aberrations in the liver of hamsters.

The derivation of RBEs from studies comparing induction of bone tumors in mammals by alpha-emitting radionuclides relative to ^{90}Sr and ^{90}Y is further complicated by differences in the distributions of the study and reference radionuclides in cortical and trabecular bone compared with bone surfaces. These differences are important because the radiosensitive tissues in bone are located near the surface. For example, ^{239}Pu appears to be approximately 15 times more effective in inducing bone tumors in mice and dogs than ^{226}Ra when toxicity is estimated based on the average skeletal dose (NCRP, 1990). However, this difference is due mainly to the fact that radium deposited in the skeleton is distributed throughout the volume of bone, as is strontium, but plutonium remains near the sites of deposition on bone surfaces. Similar effects are shown in studies of the toxicity of other alpha-emitting radionuclides in bone including, for example, ^{241}Am and $^{243,244}Cm$ (NCRP, 1990).

Estimates of RBE_M for alpha particles obtained from reviews and analyses by the NCRP (1990) and the NRPB (Muirhead et al., 1993) are summarized in Table 7. Estimates obtained in an earlier analysis by the ICRP (1980) also are summarized. The values in Table 7 are central estimates, and they vary from less than 5 to nearly 100 (see footnote b).

Based on the estimates of RBE_M in Table 7, and taking into account that there is uncertainty in each estimate, we describe the RBE factor for alpha particles at low doses and dose rates of the reference radiation, $\overline{RBE}_M$, by a stepwise-uniform probability distribution having 15% of the values in the range of 1.0-10, 25% in the range of 10-20, 30% in the range of 20-30, 20% in the range of 30-40, 7.5% in the range of 40-60, and 2.5% in the range of 60-100. This distribution has a median of 23, an arithmetic mean of 25, and a 95% confidence interval between 2.5 and 60. This probability distribution also provides a reasonable representation of the estimates of RBE_M for animal tumors only. The assumed probability distribution of $\overline{RBE}_M$ encompasses the recommended point values of the effective quality factor, $\overline{Q}$, and the radiation weighing factor, w_R, for alpha particles given Table 1.[13]

The stepwise-uniform probability distribution described above was chosen to represent the RBE factor for alpha particles based on the following considerations. The distribution of the values of RBE_M summarized in Table 7 is approximately symmetrical about a central value. The estimates of RBE_M also suggest that substantial weight should be given to values toward the extremes of the distribution, especially values toward the lower end. We give less weight to values toward the upper end of the distribution based on the consideration that estimates in the range of about 60-100 for inhalation of insoluble ^{239}Pu oxide obtained in an analysis of early studies by the ICRP (1980) were not seen in more recent studies. We also note that the

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[13]The point values of $w_R = 20$ and $\overline{Q} = 25$ in Table 1 are at the 40th and 55th percentiles, respectively, of the probability distribution of $\overline{RBE}_M$. An estimated RBE_M for inhaled alpha-emitting radionuclides of 30 derived by the ICRP (1980) from studies in animals is at the 70th percentile.

distribution of values in Table 7 is not described nearly as well by other commonly assumed probability distributions, such as lognormal or triangular. Since the probability distribution of the RBE factor has a specified lower bound of 1.0, truncation of the lower tail at 1.0 is not needed, in contrast to the case of neutrons discussed previously.

With the exception of exposure to radon and its short-lived decay products noted in the Introduction, the probability distribution of $\overline{RBE}_M$ described above is used to estimate cancer risks in humans at low doses and dose rates of alpha particles in accordance with eq. (2). Since alpha-emitting radionuclides of concern in exposures of workers and the public, excluding radon, have half-lives of at least 0.5 years and are tenaciously retained in the body, acute exposure to alpha particles emitted by inhaled or ingested radionuclides should not be of concern. External exposure generally is not a concern for alpha particles emitted by radionuclides.

Consideration of Cancer-Specific RBEs

The probability distribution of the RBE factor for alpha particles described above is intended to be applied to all cancers. There is some indication from studies in humans that the RBE for leukemia is less than the RBE for other cancers. Based on an estimated lifetime risk of leukemia of (5-6) $\times 10^{-3}$ Gy^{-1} in patients who were administered Thorotrast[14] (National Research Council, 1988) compared with an estimate of 5×10^{-3} Gy^{-1} at low doses and low dose rates of low-LET radiation, the U.S. Environmental Protection Agency (EPA) concluded that the "effective RBE" of alpha particles for leukemia is essentially unity (EPA, 1994; Eckerman et al., 1999). However, there are several possible difficulties with this interpretation. First, as noted by the EPA (1994), the lower than expected leukemia risk in the Thorotrast patients may result from a nonuniform distribution of dose within bone marrow such that average doses to sensitive target cells are substantially lower than calculated average doses to bone marrow.

Second, calculated doses to bone marrow are highly sensitive to assumptions about the distribution of alpha-emitting radionuclides on bone surfaces and in the volume of cortical and trabecular bone (Eckerman et al., 1999). This is an important consideration for ^{232}Th because thorium remains at the sites of deposition on bone surfaces but its ^{228}Ra decay product, which decays to the alpha-emitting radionuclides ^{228}Th and ^{224}Ra, is distributed in bone volume. Thus, estimated doses to bone marrow are sensitive to the assumed rate of transfer of ^{228}Ra from bone surfaces. More generally, estimates of marrow dose from alpha-emitting radionuclides deposited in the skeleton have large uncertainties that are not taken into account in the estimated risks to Thorotrast patients. For example, Hunacek and Kathren (1995) noted that reported doses to bone marrow of these patients vary by a factor of about 10, with the result that the estimated risk of leukemia ranges from 5×10^{-3} to 6×10^{-2} Gy^{-1}; the best estimate given by Hunacek and Kathren is 3×10^{-2} Gy^{-1}. Such higher risks, when compared with the estimated risk from exposure to low-LET radiation, indicate that the RBE of alpha particles is substantially greater than unity.

[14]Thorotrast is a colloidal form of thorium oxide.

Third, the estimated risk of leukemia at low doses and dose rates of low-LET radiation is based on data in the Japanese atomic-bomb survivors who received a mean absorbed dose of gamma rays of 0.25 Gy (UNSCEAR, 2000), whereas estimated doses to bone marrow from alpha particles in the Thorotrast patients are about 1 Gy or higher (National Research Council, 1988; Hunacek and Kathren, 1995). At such high doses of alpha particles, the risk of leukemia may be influenced by the effect of cell killing in bone marrow (Muirhead et al., 1993).

Finally, data on RBEs for fission neutrons discussed in the previous section do not support an assumption that the RBE for leukemias from exposure to alpha particles is less than RBEs for other cancers by a factor of 10 or more. Data on RBEs for fission neutrons are relevant because a large difference in the biological effectiveness of alpha particles and fission neutrons is not expected and has not been demonstrated experimentally (ICRU, 1986; Sinclair, 1985).

Based on these considerations and an absence of supporting information from other studies of alpha particles, we have not developed separate probability distributions of the RBE factor for leukemia and other cancers. We have accounted for the possibility of a substantially lower RBE for leukemia compared with other cancers only in a general way by defining the probability distribution of $\overline{RBE}_M$ for alpha particles so that a substantial weight is given to values in the range of 1-10.

Correction for Inverse Dose-Rate Effect

As in the case of neutrons discussed in the previous section, an additional consideration in estimating cancer risks at low doses and dose rates of alpha particles is the possibility of an inverse dose-rate effect, whereby the biological effectiveness at a given dose increases as the dose rate decreases. An analysis of data in humans (underground miners) who were exposed to elevated levels of radon has shown an inverse dose-rate effect that could be as much as a factor of 3 but is more likely less than a factor 2 (Lubin et al., 1995).

Arguments can be made both for and against the need to account for a possible inverse dose-rate effect in estimating cancer risks from chronic exposure to alpha particles. An argument in favor is that since an inverse dose-rate effect has been observed in some studies of neutrons, the effect, if it exists, also should occur with other high-LET radiations. However, there are several counter-arguments to this view. First, an inverse dose-rate effect is not observed in underground miners at exposures to radon decay products less than 50 Working Level Months (WLM) (Lubin et al., 1995).[15] Second, in contrast to studies of neutrons in small mammals, all studies using alpha-emitting radionuclides involved protracted exposures, and the estimated RBEs may already account for an inverse dose-rate effect. Finally, again in contrast to neutrons, the RBEs for alpha particles are extrapolated values at low doses and dose rates, RBE_M, and the

[15]Based on conversion coefficients given in Table 4 of ICRP (1987) and Table 6 of ICRP (1993), an exposure of 50 WLM corresponds to an absorbed dose to the bronchial epithelium, where lung carcinomas in the underground miners are observed to originate, of about 0.8 Gy.

highest values, which correspond to the highest DDREFs of the reference low-LET radiations, may result in overestimates of cancer risks in humans.

Based on these arguments, we assume that the probability distribution of the RBE factor for alpha particles described previously should be adjusted by a small factor that represents the inverse dose-rate effect, to be consistent with an assumption of this effect in cases of chronic exposure to neutrons. However, we give less weight to a possible inverse dose-rate effect for alpha particles than for neutrons based mainly on two considerations discussed above. First, the data on underground miners do not show an effect at low doses of concern in routine exposures of workers and the public. Second, the probability distribution of the RBE factor may already incorporate an inverse dose-rate effect when the relevant studies involved protracted exposures to alpha particles. Specifically, we assume a discrete probability distribution for the enhancement factor representing the inverse dose-rate effect for alpha particles with 70% of the values at 1.0, 20% at 1.5, 7.5% at 2.0, and 2.5% at 3.0. The arithmetic mean of this distribution is about 1.2.

Summary

Cancer risks in humans from exposure to alpha particles emitted by radionuclides are estimated using an approach represented by eq. (2). Specifically, the risk per unit absorbed dose from exposure to alpha particles (α) is estimated as

$$R_\alpha = \overline{\mathrm{RBE}}_{\alpha,\mathrm{M}} \times \mathrm{EF}_\alpha \times \frac{R_{\gamma,\mathrm{H}}}{\mathrm{DDREF}_\gamma}, \qquad (6)$$

where $\overline{\mathrm{RBE}}_{\alpha,\mathrm{M}}$ is the RBE factor for alpha particles at low doses and dose rates, EF_α is an enhancement factor that represents the inverse dose-rate effect for chronic exposure to alpha particles, $R_{\gamma,\mathrm{H}}$ is the risk per unit dose at high doses and high dose rates of gamma rays, and DDREF_γ is the dose and dose-rate effectiveness factor for gamma rays and other low-LET radiations. Since exposures to alpha-emitting radionuclides are assumed to be chronic, the enhancement factor is applied in all such cases. Truncation of the aggregate probability distribution of $\overline{\mathrm{RBE}}_{\alpha,\mathrm{M}} \times \mathrm{EF}_\alpha$ at 1.0, consistent with the approach for neutrons discussed previously, is not needed, because this distribution does not include values less than 1.0. As noted in the Introduction, eq. (6) applies to all exposures to alpha particles emitted by radionuclides, except inhalation of radon and its short-lived decay products.

RBE FACTORS FOR PHOTONS

Approach to Estimating RBEs

Compared with neutrons, alpha particles, and beta particles from decay of ^{3}H, there are few measurements of the biological effectiveness of orthovoltage *X* rays (and other lower-energy

photons) relative to high-energy gamma rays. Furthermore, a review by the NCRP (1990) indicates that only a single stochastic endpoint in mammalian systems (induction of dicentric chromosomes in human lymphocytes) has been widely studied in investigating the biological effectiveness of *X* rays. Nonetheless, we believe that the available data on chromosome aberrations, supplemented by information obtained from studies of other radiations discussed in this section, provide sufficient evidence to support an assumption that lower-energy photons have a substantially greater biological effectiveness than high-energy gamma rays. As noted in the Introduction, the ICRU (1986) reached the same conclusion. This assumption applies to orthovoltage *X* rays and other photons of similar energies including, for example, the 60-keV gamma ray emitted in decay of ^{241}Am.

In estimating cancer risks in humans from exposure to X rays and other lower-energy photons, the approach represented by eq. (2), which applies at low doses and low dose rates, is used. An analysis to estimate RBEs at high doses and high dose rates of photons, $RBE_{\gamma,H}$, similar to the analysis for neutrons by Edwards (1997; 1999) discussed previously, has not, to our knowledge, been performed. An additional complication that discourages the use of RBEs at high doses and high dose rates and an approach to estimating risks represented by eq. (3) is that the reference gamma rays and the *X* rays under study both exhibit non-linear dose-response relationships. As a consequence, the DDREFs for the two radiations in a given study often differ substantially from each other and from the nominal value of 2 normally used in radiation protection (ICRP, 1991; NCRP, 1993), and the DDREFs for the two radiations also vary from one study to another. Therefore, the following discussion focuses on the estimation of RBEs for lower-energy photons at low doses and low dose rates, $RBE_{\gamma,M}$.

Development of RBE Factor

Studies of the biological effectiveness of 220-250 kVp *X* rays in inducing dicentric chromosomes in human lymphocytes were reviewed and evaluated by the NCRP (1990). The average *X*-ray energy in these studies was about 50-65 keV (Stanton et al., 1979; NCRP, 1985). The dose-response relationships for the *X* rays and reference gamma rays in these studies were assumed to be linear-quadratic; i.e., the response was assumed to be described by $\alpha D + \beta D^2$, where D is the absorbed dose and α and β are coefficients obtained from fits to the data. The data on dose-response for the *X* rays and reference gamma rays in the various studies are summarized in Table 8. Point estimates of RBE_M, calculated by the NCRP (1990) as α_X/α_γ using the central estimates of the two coefficients in Table 8, are given in Table 9. Similar values of RBE_M for *X* rays are indicated when estimates of RBE_M for neutrons for the same endpoint obtained in studies using *X* rays as the reference radiation are compared with estimates obtained using ^{60}Co gamma rays (Dobson et al., 1991; Schmid et al., 2000).

The NCRP's point estimates of RBE_M in Table 9 do not take into account the reported uncertainties in the coefficients α_X and α_γ. We estimated the uncertainty in each value of RBE_M in the following way. We assumed that the central estimates and standard errors of α_X and α_γ given in Table 8 define 68% confidence intervals of lognormal probability distributions of these

coefficients.[16] We then used random sampling methods to calculate the probability distribution of RBE_M as the ratio of the distributions of α_X and α_γ, and the 68% confidence interval of this distribution was obtained. These confidence intervals are given in parentheses in Table 9.

The estimates of RBE_M for *X* rays and their uncertainties summarized in Table 9 can be represented reasonably well by a lognormal probability distribution having a 95% confidence interval between 1.0 and 6.5. However, information obtained from other studies also should be taken into account. This information is indirect, in that the radiation under study was not *X* rays or gamma rays but both of these radiations were used as reference radiations. Inferences about the biological effectiveness of *X* rays relative to gamma rays can be made by comparing RBEs for the radiation under study relative to *X* rays with RBEs relative to gamma rays, provided the values apply to similar endpoints. Information obtained from various studies, mostly reviews by experts and expert groups, is summarized below.

- A study of induced pink mutation events in stamen hairs of *Tradescantia* (Underbrink et al., 1970) discussed in Section 2.2.4 of NCRP (1990), in which the radiations under study were neutrons, indicated that the RBE of *X* rays was about 1.7.

- Studies of mutations in human diploid fibroplasts (Cox et al., 1977; Hei et al., 1988) summarized in Fig. 3.13 of NCRP (1990), in which the radiations under study included protons, deuterons, and ions of ^3He, ^4He, ^{10}B, and ^{14}N, indicated that the RBE of *X* rays was about 3 or less.

- A study of dominant lethal mutations in cells of mice (Pomerantseva, 1964) discussed in Section 4.1.1.1 of NCRP (1990), in which the radiation under study was high-energy protons, indicated that the RBE of *X* rays was about 1.5.

- A study of life-shortening in mice (Upton et al., 1967) summarized in Table 8.2 of NCRP (1990), in which the radiations under study were neutrons, indicated that the RBE at low doses and low dose rates of *X* rays was about 3 or less. A similar result was obtained from an analysis of these data by Edwards (1999) to obtain estimates of RBE for neutrons at high acute doses of the reference radiation, RBE_H (see Table 3).

- A study of mutations in human lung fibroplasts (Cox and Masson, 1979) summarized in Section 7, Paragraph 19, and Table 7.3 of Muirhead et al. (1993), in which the radiations under study were alpha particles, indicated that the RBE of *X* rays was about 2.5 when compared with the results of a study of mutations in Chinese hamster cells (Thacker et al., 1979) summarized in Table 7.

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[16]Uncertainties are described by lognormal probability distributions to avoid problems that arise in calculating the ratio of two normal distributions when very small or negative values of the probability distribution in the denominator are randomly sampled.

- Several inferences can be made from studies of the biological effectiveness of low-energy beta particles from ^3H decay summarized by Straume and Carsten (1993) and discussed in the following section. Studies of carcinogenesis endpoints in mammals and mammalian cells indicated that the RBE of *X* rays was less than 2 (see Table 10). Studies of genetic endpoints in mammalian systems and fish lymphocytes indicated that the RBE of *X* rays was about 1.6 on average and did not exceed about 3.5 (see Table 11). A study of chromosome aberrations in human lymphocytes indicated that the 68% confidence interval of the RBE for *X* rays was (2.3, 3.9) (see Table 12); this estimate applies to the same endpoint as the results summarized in Table 9. Results of studies of reproductive effects in small mammals and fish summarized in Table 7 of Straume and Carsten (1993) are not considered, because these endpoints are deterministic and, thus, are not considered to be relevant in estimating cancer risks in humans.

- A study of tumor induction in rats (Wolf et al., 2000), in which the radiation under study was fission neutrons, indicated that the RBE of *X* rays at acute doses of 2 Gy was about 3. This RBE should be especially relevant to estimating cancer risks in humans.

The indirect estimates of RBE summarized above suggest that a lognormal probability distribution of RBE_M for *X* rays and other lower-energy photons having a 95% confidence interval between 1.0 and 6.5 gives too much weight to relatively high values. We believe that this conclusion is reasonable even though uncertainties in the indirect estimates undoubtedly are substantial. We also note that the highest values of RBE_M in Table 9 have the largest uncertainties, which indicates that these values should be given less weight compared with the lower, and less uncertain, estimates of RBE_M for the same endpoint. Based on this information, we reduce the upper confidence limit of the lognormal probability distribution of RBE_M obtained from studies of dicentric chromosomes in human lymphocytes from 6.5 to 5.0. Thus, the lognormal probability distribution of RBE_M that is assumed to describe all the radiobiological data discussed above has a 95% confidence interval between 1.0 and 5.0. This distribution has a geometric mean and geometric standard deviation of 2.2 and 1.5, respectively, and an arithmetic mean of 2.4. The distribution assigns a small weight to an assumption that the biological effectiveness of *X* rays and other lower-energy photons is the same as that of high-energy gamma rays, and to an assumption that values greater than 5 are possible. Neither of these assumptions can be ruled out by the available radiobiological data.

We then investigated whether useful information on the biological effectiveness of *X* rays relative to high-energy gamma rays can be obtained from epidemiological studies of human populations. In particular, estimated risks of thyroid cancer in children exposed to *X* rays can be compared with estimated risks of thyroid cancer in the Japanese atomic-bomb survivors who were exposed in childhood mainly to high-energy gamma rays. For the atomic-bomb survivors, the following central estimates and 95% confidence intervals (in parentheses) of the excess relative risk of thyroid cancer per Gy in children have been reported:

- 4.7 (1.7, 11) – atomic-bomb survivors less than 15 years old at time of exposure, with a mean thyroid dose from gamma rays of 0.27 Gy (Ron et al., 1995);
- 9.5 (4.1, 19) – atomic-bomb survivors less than 10 years old at time of exposure, with the same mean thyroid dose (Thompson et al., 1994).

These estimates indicate that the risk to children of age less than 10 years at time of exposure is substantially greater than the risk to children of age 10-15 years. For children exposed to *X* rays, the following excess relative risks of thyroid cancer per Gy have been reported (Ron et al., 1995):

- 9.1 (3.6, 29) – newborn children in Rochester, New York, treated for enlarged thymus gland at ages less than 1 year, with a mean thyroid dose from *X* rays of 1.4 Gy;
- 33 (14, 57) – Israeli children treated for ringworm of the scalp at a mean age of 7 years, with a mean thyroid dose from *X* rays of 0.09 Gy;
- 2.5 (0.6, 26) – children in Chicago, Illinois, treated for enlarged tonsils and adenoids at ages 0-15 years (mean age of 4 years), with a mean thyroid dose from *X* rays 0.59 Gy;
- 7.7 (2.1, 29) – pooled analysis of data on childhood exposures at ages 0-15 years, including data on the atomic-bomb survivors (result is dominated by data on childhood exposures to *X* rays at ages less than 10 years).

An RBE for *X* rays can be estimated from these results by assuming that the probability distribution of the estimated risk in each study is lognormal and calculating ratios of the probability distributions for *X* rays to the distributions for gamma rays. Given that the average ages of the children exposed to *X* rays was 7 years or less, the estimated risk in the atomic-bomb survivors of age less than 10 years is used to estimate RBEs. The 95% confidence intervals of the RBEs obtained from the three separate studies of children exposed to *X* rays are (0.3, 4.2), (1.1, 9.2), and (0.06, 3.5), and the 95% confidence interval obtained using the results of the pooled analysis is (0.2, 4.0). If we assume that the biological effectiveness of *X* rays in humans should not be less than that of high-energy gamma rays, based on the calculated effective quality factor in Fig. 1 (ICRU, 1986), these confidence intervals indicate that the RBE for *X* rays in inducing thyroid cancer in children most likely is in the range of about 1-4.

Additional information on the RBE for *X* rays in inducing thyroid cancer can be obtained from a study in prepubescent rats exposed to *X* rays and beta particles emitted in ^{131}I decay (Lee et al., 1982). The biological effectiveness of ^{131}I beta particles, which have an average energy of 182 keV (Kocher, 1981), should be similar to that of high-energy gamma rays (see discussion in section on RBE factors for electrons). The following central estimates and 95% confidence intervals (in parentheses) of ratios of thyroid tumor incidence from *X* rays to that from ^{131}I beta particles at different mean thyroid doses were obtained: 1.1 (0.32, 3.7) at 0.8 Gy, 1.2 (0.43, 3.2) at 3.3 Gy, and 1.4 (0.24, 7.6) at 8.5 Gy. If the three confidence intervals are averaged, the result is a central estimate (50th percentile) and 95% confidence interval of 1.4 (0.6, 3.6). Thus, although the uncertainties are large and an RBE as high as about 4 cannot be ruled out, the biological effectiveness of *X* rays and ^{131}I beta particles in inducing thyroid cancer in the study animals was about the same, on average.

Finally, we examined results obtained from epidemiological studies of cancers at other sites, including the colon, lung, skin, female breast, and bladder (UNSCEAR, 2000). The central estimate of the excess relative risk per Gy in populations exposed to *X* rays often was comparable to or less than the central estimate in a similar age group in the atomic-bomb survivors, although some of the lower risks from *X* rays may be influenced by the much higher doses of *X* rays compared with the doses of gamma rays in the atomic-bomb survivors. In those few cases where a higher risk was observed in populations exposed to *X* rays, the difference was less than a factor of 2. In all cases, however, uncertainties in the risk estimates are sufficiently large that an RBE for *X* rays substantially greater than 1 cannot be ruled out.

The results of epidemiological studies described above lead to the following observations. First, there is no evident difference in the effectiveness of *X* rays in inducing thyroid cancers compared with cancers at other sites. Second, the uncertainties in the results of epidemiological studies are sufficiently large that an upper confidence limit of the RBE factor as high as 5.0, as we have assumed based on radiobiological studies, cannot be ruled out. Third, although uncertainties in the results of epidemiological studies are large, in no cases is a central estimate of an RBE for *X* rays as high as 4 obtained. Based on considerations of statistical uncertainties alone, an occasional high estimate of RBE would be expected. Finally, the epidemiological data do not rule out an assumption that the biological effectiveness *X* rays in inducing cancers in humans is the same as that of high-energy gamma rays.

Based on the evidence obtained from all the radiobiological and epidemiological studies discussed above, we describe the RBE factor for orthovoltage *X* rays and other lower-energy photons, $\overline{\mathrm{RBE}}_{\mathrm{M}}$, to be used in estimating cancer risks at low doses and low dose rates in accordance with eq. (2) by a probability distribution in which a weight of 0.25 is assigned to the value 1.0 and a weight of 0.75 is assigned to a lognormal distribution having a 95% confidence interval between 1.0 and 5.0. That is, we use the results of epidemiological studies to modify the lognormal probability distribution that was based on the results of radiobiological studies by assigning a substantial weight to an assumption that *X* rays and other lower-energy photons have the same biological effectiveness in humans as high-energy gamma rays. The resulting probability distribution of the RBE factor has a 95% confidence interval between 1.0 and 4.7. The 50$^{\mathrm{th}}$ percentile of this distribution is 1.9, and the arithmetic mean is 2.1.

Energy-Dependence of RBE Factor

Based on a calculation of the effective quality factor vs. photon energy given in Fig. 1 (ICRU, 1986), we assume that the RBE factor for orthovoltage *X* rays and other lower-energy photons described above applies at energies of 30-250 keV; the effective quality factor is essentially independent of energy over much of this range. We also note that the effective quality factor at these energies is slightly more than twice the value at the energies of ^{60}Co gamma rays (1.2 and 1.3 MeV); by our reading of the curve in Fig. 1, the difference is a factor of 2.3. This result is in good agreement with the central estimate of the RBE factor described above and, thus, provides support for our assumption.

An assumption that the RBE factor applies at photon energies as low as 30 keV is supported by calculations of the biological effectiveness of 60- and 80-kVp *X* rays relative to gamma rays from the Hiroshima and Nagasaki atomic bombs for a number of specific endpoints, including chromosomal aberrations in human lymphocytes, induction of mutations in human fibroblasts, and oncongenic transformation in C3H10T½ mouse cells (Brenner, 1999). RBEs at low doses between 1.6 and 2.0 were calculated. The differences between these values and the value of 2.3 inferred from the calculation in Fig. 1 are due, in part, to differences in the assumed responses as a function of lineal energy and to an assumption that the average energies of gamma rays from the atomic bombs were somewhat less than the energies of ^{60}Co gamma rays. The biological effectiveness of photons of energy less than 30 keV is considered below.

The calculation of the effective quality factor shown in Fig. 1 indicates that the biological effectiveness increases as the photon energy decreases below 30 keV. For example, using the calculation in Fig. 1, Brenner and Amols (1989) estimated that 23 kVp *X* rays should be approximately 1.3 times more effective than 44-250 kVp *X* rays in inducing breast cancer. Thus, based on the calculation in Fig. 1, we assume that the probability distribution of the RBE factor for photons of energy 30-250 keV should be increased when the energy is less than 30 keV, and we represent this increase by a factor which is described by a triangular probability distribution having a lower bound of 1.0, a mode of 1.3, and an upper bound of 1.6.

Summary

Cancer risks in humans from exposure to photons are estimated using an approach represented by eq. (2). Specifically, the risk per unit absorbed dose from exposure to photons (γ) at low doses and low dose rates is estimated as

$$R_\gamma = \overline{\mathrm{RBE}}_{\gamma,\mathrm{M}} \times \mathrm{AF}_\gamma \times \frac{R_{\gamma,\mathrm{H}}}{\mathrm{DDREF}_\gamma}, \qquad (7)$$

where $\overline{\mathrm{RBE}}_{\gamma,\mathrm{M}}$ is the RBE factor for photons of energy 30-250 keV at low doses and low dose rates, AF_γ is an adjustment factor that represents an increase in biological effectiveness when the photon energy is less than 30 keV, and $R_{\gamma,\mathrm{H}}$ and DDREF_γ are the same as in eq. (2). The relative biological effectiveness of all photons of energy greater than 250 keV is assumed to be unity.

Given the assumed probability distributions of $\overline{\mathrm{RBE}}_{\gamma,\mathrm{M}}$ at energies of 30-250 keV and the adjustment factor, AF_γ, at energies less than 30 keV, a small probability is assigned to an RBE factor less than 1.0 at energies less than 250 keV. In all such cases, however, the lower tail of the probability distribution of the RBE factor should be truncated at 1.0. This truncation is based on the calculated effective quality factor in Fig. 1, which indicates that the biological effectiveness of lower-energy photons should not be less than that of high-energy gamma rays.

Acute exposure to photons also is of concern in exposures of workers and the public. Cancer risks in humans from acute exposure to photons also are estimated using eq. (7), and the two terms describing the biological effectiveness of photons of energy less than 250 keV relative to high acute doses of high-energy gamma rays are the same. However, the dose and dose-rate effectiveness factor ($DDREF_\gamma$) is different, and generally lower, than in cases of chronic exposure. The probability distribution of $DDREF_\gamma$ for acute exposure is assumed to depend on the magnitude of the dose, and a single value of 1.0 is assumed at absorbed doses above 0.2 Gy (see footnote a in Table 14). Thus, the biological effectiveness of lower-energy photons relative to high-energy gamma rays is assumed to be independent of dose and dose rate under similar conditions of exposure to the two radiations.

RBE FACTORS FOR ELECTRONS

With the exception of the low-energy electrons emitted in beta decay of ^3H, there have been few studies of the biological effectiveness of electrons relative to gamma rays or *X* rays. In this section, we first develop a probability distribution of the RBE factor for beta particles emitted in ^3H decay. The spectrum of electrons in ^3H decay has an average energy of 5.7 keV and a maximum energy of 18.6 keV (Kocher, 1981). We then consider the biological effectiveness of other electrons, including low-energy Auger electrons.

RBE Factor for Tritium Beta Particles

Many studies have shown that beta particles emitted in ^3H decay are biologically more effective than gamma rays in inducing stochastic effects (NCRP, 1990; Straume and Carsten, 1993). Estimates of RBE obtained from studies reviewed by Straume and Carsten (1993), including studies in which the reference radiation was *X* rays, are summarized in Tables 10-13.

For purposes of estimating an RBE factor for ^3H beta particles that is consistent with the RBE factors developed for the other radiation types, the relevant studies are those in which the reference radiation was gamma rays. In most studies using gamma rays, the reference radiation was delivered chronically to match the conditions of exposure to ^3H beta particles. Thus, cancer risks in humans per unit dose of ^3H beta particles are estimated using the approach in eq. (2), which applies at low doses and dose rates. If we assume that the DDREF for ^3H beta particles in the various studies is about the same as the DDREF for the reference radiation, RBEs obtained under conditions of chronic exposure in Tables 10-13 provide estimates of RBE_M.

Based on the RBEs for chronic or sub-acute exposure to gamma rays in Tables 10-13, we describe the RBE factor for ^3H beta particles at low doses and low dose rates, $\overline{RBE}_M$, by a lognormal probability distribution having a 95% confidence interval between 1.2 and 6.0. This distribution has a geometric mean and geometric standard deviation of 2.7 and 1.5, respectively, and an arithmetic mean of 2.9. Given the residence half-time of tritiated water in soft tissues of

about 10 days (ICRP, 1979) and the much longer half-life of ^{3}H (12.3 years), acute exposure to beta particles emitted by ^{3}H is not expected to be of concern.

In a previous analysis by *SENES* Oak Ridge (Thomas and Hoffman, 2000), the RBE factor for ^{3}H beta particles was described by a triangular probability distribution having a lower bound of 1.0, a mode of 2.0, and an upper bound of 5.0. The lognormal probability distribution described above is similar to the previous assumption. However, based on the data summarized in Tables 10-13, an RBE greater than 5 cannot be ruled out. The upper tail of the lognormal probability distribution represents an assumption that the RBE factor could be 5 or greater, and that a reasonable upper bound cannot be determined with certainty. The substantial probability assigned to an RBE factor of 4 or greater (about 15%) also is intended to take into account that the RBE for organically-bound tritium appears to be 2-3 times higher than the RBE for HTO or ^{3}H incorporated into amino acids (see Tables 11 and 13). This is an important consideration when some HTO taken into the body becomes organically-bound before it is excreted (Straume and Carsten, 1993).

The assumed probability distribution of the RBE factor for ^{3}H beta particles is nearly the same as the probability distribution for photons of energy less than 30 keV discussed in the previous section. This consistency is expected when, as discussed below, the energies of electrons that deliver an absorbed dose are similar. The assumed probability distribution also is supported by the data in Tables 10-13 which indicate that biological effectiveness of ^{3}H beta particles is about the same as that of *X* rays.

RBE Factor for Other Electrons

Since the energies of ^{3}H beta particles are very low, we considered whether other electrons, especially those of higher energy, should be assigned an RBE factor greater than unity. In radiation protection, all such electrons generally are assumed to have the same biological effectiveness as high-energy gamma rays (see Table 1). The study of the biological effectiveness of *X* rays and beta particles from ^{131}I decay in inducing thyroid cancer in rats by Lee et al. (1982) discussed previously is the only study we are aware of that was specifically designed to investigate the biological effectiveness of higher-energy electrons. In the absence of extensive radiobiological data, we address this question using the following arguments.

In the previous section, data on the biological effectiveness of *X* rays and a calculation of the effective quality factor vs. photon energy shown in Fig. 1 were used to develop RBE factors greater than 1.0 for photons of energy less than 250 keV. Since the absorbed dose from irradiation by photons is due almost entirely to energetic secondary electrons produced by interactions of the photons in tissue, information on the biological effectiveness of photons can be used to infer the biological effectiveness of electrons. That is, an RBE factor for photons of a given energy essentially describes the biological effectiveness of the secondary electrons produced by the first interactions of these photons in tissue.

The energies of secondary electrons produced by interactions of photons in tissue generally decrease with decreasing photon energy. Therefore, electrons produced by interactions of 250-keV photons in tissue are at the highest energies for which the biological effectiveness should be the same as that of lower-energy photons. In tissue, which has an average atomic number of 7 (Shleien et al., 1998), Compton scattering is the dominant interaction at a photon energy of 250 keV [see Fig. A.1 of NCRP (1991) and Figs. 5.1 and 5.2 of Shleien et al. (1998)]. At this energy, the spectrum of secondary electrons produced by Compton scattering has a maximum energy of 124 keV and an average energy of 60 keV (Turner, 1995). In contrast, the energy of secondary electrons produced by the photoelectric effect in tissue at this energy is nearly 250 keV, since the binding energies of electrons in atoms of the elements comprising tissue are about 3 keV or less (Shleien et al., 1998). At 250 keV, however, photoelectrons are produced in only about 0.1% of all interactions [see Fig. 5.2 of Shleien et al. (1988)] and, thus, have little effect on the average energy of secondary electrons.

As the incident photon energy decreases below 250 keV, the photoelectric effect increases in importance relative to Compton scattering, and becomes the dominant interaction in tissue at energies less than about 30 keV (Schleien et al., 1998; NCRP, 1991). At this energy, the average and maximum energies of secondary electrons in Compton scattering are about 1.5 and 3 keV, respectively, and the average energy of photoelectrons is nearly 30 keV. Thus, the average energy of secondary electrons at this photon energy is about 15 keV. This result is of interest because we have assumed, based on the calculated effective quality factor shown in Fig. 1, that the biological effectiveness of photons of energy less than 30 keV is higher than at 30-250 keV. Thus, the same increase should apply to electrons of energy less than about 15 keV. As the photon energy decreases below 30 keV, the energies of secondary electrons produced in tissue approach the incident photon energy, due to the increasing dominance of the photoelectric effect and the low binding energies of atomic electrons in tissue. At a photon energy of 20 keV, for example, the energies of secondary electrons are little different from the photon energy.

We believe that three conclusions can be drawn from this analysis. First, at electron energies greater than 60 keV, the RBE factor can be assumed to be unity, without uncertainty, to conform to the assumption for photons of energy greater than 250 keV. Second, at electron energies in the range of 15-60 keV, the RBE factor can be assumed to be the same as the RBE factor for photons of energy 30-250 keV. Third, at electron energies less than 15 keV, but possibly excluding low-energy Auger electrons as discussed below, the RBE factor can be assumed to be the same as the RBE factor for photons of energy less than 30 keV.

At electron energies less than 15 keV, however, we believe it is preferable to assume that the RBE factor is the same as the RBE factor for beta particles emitted in ^{3}H decay. As noted above, the RBE factors for ^{3}H beta particles and photons of energy less than 30 keV are nearly the same. In our view, an advantage of using the RBE factor for ^{3}H beta particles is that it is based directly on radiobiological data. We also note that the energies in the spectrum of ^{3}H beta particles span the energies over which the RBE factor at the lowest electron energies is applied.

The appropriate RBE factor at electron energies of 15-60 keV or less than 15 keV should be applied to beta-emitting radionuclides when the average energy of the continuous spectrum of beta particles is less than 60 keV. Use of the average energy of beta particles is reasonable when the argument to assume an RBE factor greater than 1.0 at energies less than 60 keV is based on the average energy of the continuous spectrum of secondary electrons in Compton scattering. The appropriate RBE factor also should be applied to discrete internal conversion electrons of energy less than 60 keV emitted by radionuclides.[17] In these cases, however, an RBE factor needs to be taken into account only when the average energy of low-energy internal conversion electrons per decay of a radionuclide is significant compared with the average energies per decay of other radiations having a short range in tissue, including internal conversion electrons of energy greater than 60 keV, beta particles, and alpha particles. Application of the RBE factors to Auger electrons is discussed below.

RBE Factors for Auger Electrons

Radionuclides that emit Auger electrons[18] require special consideration, due to the very low energies of these radiations (often a few keV or less) and their short range in matter (less than 0.1 μm). The ICRP (1991) and the NCRP (1993) recommend that Auger electrons emitted by radionuclides that are incorporated into DNA should not be assigned a radiation weighting factor of 1 (see Table 1), since it is unreasonable to average the absorbed dose over the whole mass of DNA. Techniques of microdosimetry are considered more appropriate in such cases.

Limited data on the biological effectiveness of Auger electrons are summarized by the ICRP (1991). When Auger emitters penetrate a cell but are not incorporated into DNA, RBEs for a number of endpoints, including cell killing, are in the range of 1.5-8. Such RBEs are similar to values for low-energy beta particles from ^{3}H decay discussed previously. However, when Auger emitters, such as ^{125}I, are incorporated into DNA, RBEs in the range of 20-40 have been found for such endpoints as cell transformation. Such high RBEs are supported by calculated patterns of energy deposition.

When information on whether an Auger-emitting radionuclide is incorporated into DNA of an exposed individual is lacking, we believe that Auger electrons should be treated in the same

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[17]Internal conversion is the process by which the energy difference between an initial and final state in an atomic nucleus is transferred directly to a bound atomic electron, which is then ejected from the atom. The emission of internal conversion electrons competes with the emission of gamma rays, and it increases in importance as the atomic number increases.

[18]The emission of Auger electrons competes with the emission of *X* rays as a means of carrying off the energy released when a vacant energy state of electrons in an atom is filled by an electron in a higher energy state. In the Auger process, the filling of the vacant energy state is accompanied by the simultaneous ejection of an electron in a higher energy state from the atom. Auger electrons usually are important only when a radionuclide decays by electron capture or an isomeric transition (Kocher, 1981).

way as other low-energy electrons. Thus, for example, when the energy of Auger electrons is less than 15 keV, the RBE factor that applies to low-energy beta particles emitted in ^{3}H decay should be used. When Auger electrons are important compared with other low-energy electrons, their energies are nearly always less than 15 keV (Kocher, 1981).

When an Auger-emitting radionuclide is known to be incorporated into DNA, however, we do not believe that a credible probability distribution of the RBE factor can be developed based on available information. Although the RBE factor in such cases should be substantially higher than the RBE factor that applies to ^{3}H beta particles, there are potentially important uncertainties including, for example, the fraction of the activity that is incorporated into DNA, the dependence of RBE on the energy of Auger electrons, and the dependence of RBE on dose when cell killing could occur. Thus, we support the recommendation of the ICRP (1991) and the NCRP (1993) that the biological effectiveness of Auger emitters that are incorporated into DNA should be handled as special cases using techniques of microdosimetry.

Summary

Cancer risks in humans from exposure to electrons are estimated using an approach represented by eq. (2). Specifically, the risk per unit absorbed dose of electrons (e) at low doses and low dose rates is estimated as

$$R_e = \overline{\mathrm{RBE}}_{e,\mathrm{M}} \times \frac{R_{\gamma,\mathrm{H}}}{\mathrm{DDREF}_\gamma}, \tag{8}$$

where $\overline{\mathrm{RBE}}_{e,\mathrm{M}}$ is the RBE factor for electrons at low doses and low dose rates, and $R_{\gamma,\mathrm{H}}$ and DDREF_γ are the same as in eq. (2). Two RBE factors are specified. The first applies to electrons of energy 15-60 keV, including spectra of beta particles for which the average energy lies in this range. At these energies, the RBE factor is assumed to be the same as the RBE factor for photons of energy 30-250 keV, based on considerations of the energies of secondary electrons produced by interactions of these photons in tissue. At electron energies less than 15 keV, including spectra of beta particles of the appropriate average energy, an RBE factor obtained from radiobiological data on beta particles emitted in decay of ^{3}H is applied, except when an Auger-emitting radionuclide is known to be incorporated into DNA. The relative biological effectiveness of all electrons of energy greater than 60 keV is assumed to be unity. This assumption applies, for example, to the spectrum of beta particles emitted in ^{131}I decay.

Given the assumed probability distributions of $\overline{\mathrm{RBE}}_{e,\mathrm{M}}$ at energies of 60 keV or less, a small probability is assigned to an RBE factor less than 1.0. In all cases, however, the lower tail of the probability distribution of the RBE factor should be truncated at 1.0. This truncation is based on an assumption that the biological effectiveness of low-energy electrons should not be less than that of high-energy gamma rays, and it is consistent with the truncation of probability distributions of RBE factors for lower-energy photons discussed previously.

The assumed RBE factors for electrons would be important in calculating cancer risks and probability of causation whenever intakes of radionuclides that emit low-energy beta particles, internal conversion electrons, or Auger electrons contribute significantly to estimated doses to an organ or tissue of concern. Examples of potentially important radionuclides that emit electrons in the energy range of 15-60 keV include ^{14}C, ^{63}Ni, ^{93}Zr and its decay product ^{93m}Nb, ^{95}Nb, ^{129}I, ^{132}Te, and ^{151}Sm (Kocher, 1981). At energies less than 15 keV, potentially important radionuclides include, in addition to ^{3}H, the beta-emitting radionuclides ^{106}Ru and ^{107}Pd and the Auger-emitting radionuclides ^{51}Cr, ^{55}Fe, ^{57}Co, ^{58}Co, ^{65}Zn, and ^{125}I (Kocher, 1981).

If acute exposure to electrons is of concern, the dose and dose-rate effectiveness factor ($DDREF_\gamma$) is estimated as in cases of acute exposure to photons discussed following eq. (7). Acute exposure to electrons could be important in cases of external exposure, but is unlikely to be important in cases of internal exposure to radionuclides.

SUMMARY OF RBE FACTORS FOR DIFFERENT RADIATIONS

Based on evaluations of information on the biological effectiveness of various types of ionizing radiation, we have developed relative biological effectiveness (RBE) factors for use in calculating the probability of causation of specific cancers in humans. These RBE factors are applied to estimates of cancer risks per unit dose at high doses and high dose rates of high-energy gamma rays, which are obtained mainly from studies in the Japanese atomic-bomb survivors.

The RBE factors developed in this report are expressed as probability distributions. These distributions are intended to represent the current state of knowledge (i.e., uncertainties) in the relevant radiobiological data and any other judgments involved in evaluating the available information. The RBE factors for the different radiations considered in this report are summarized as follows.

Neutrons

Cancer risks per unit absorbed dose at any dose and dose rate of neutrons are estimated using eq. (5). At energies in the range of 0.1-2 MeV, including fission neutrons, the RBE factor at high doses and high dose rates of the reference gamma radiation, $\overline{RBE}_{n,H}$, is described by a lognormal probability distribution having a 95% confidence interval between 1.5 and 30. This distribution has a geometric mean of 6.7 and a geometric standard deviation of 2.2.

At energies outside the range of 0.1-2 MeV, the RBE factor is obtained by scaling (reduction) of the probability distribution of $\overline{RBE}_{n,H}$ by an adjustment factor which is based mainly on the energy dependence of the radiation weighting factor recommended by the ICRP (1991). At energies of 10-100 keV or 2-20 MeV, this adjustment factor is described by a lognormal probability distribution having a 95% confidence interval between 1.0 and 4.0; at energies of <10 keV or >20 MeV, this adjustment factor is described by a lognormal probability

distribution having a 95% confidence interval between 2.0 and 8.0. These distributions have a geometric mean of 2.0 and 4.0, respectively, and a geometric standard deviation of 1.4.

Under conditions of chronic exposure only, a small enhancement factor representing a possible inverse dose-rate effect is applied to the RBE factor for neutrons of any energy. This enhancement factor is described by a discrete probability distribution having 50% of the values at 1.0, 30% at 1.5, 15% at 2.0, and 5% at 3.0.

After all relevant adjustments for the exposure situation of concern are applied to the RBE factor for fission neutrons, $\overline{\text{RBE}}_{n,\text{H}}$, the lower tail of the resulting probability distribution should be truncated at 1.0. This truncation is based on an assumption that the biological effectiveness of neutrons should not be less than that of high-energy gamma rays.

Alpha Particles

Except in cases of exposure to radon and its short-lived decay products, cancer risks per unit absorbed dose at low doses and low dose rates of alpha particles are estimated using eq. (6). The RBE factor at low doses and low dose rates of the reference gamma radiation, $\overline{\text{RBE}}_{\alpha,\text{M}}$, is described by a stepwise-uniform probability distribution having 15% of the values in the range of 1.0-10, 25% in the range of 10-20, 30% in the range of 20-30, 20% in the range of 30-40, 7.5% in the range of 40-60, and 2.5% in the range of 60-100. A small enhancement factor representing a possible inverse dose-rate effect is applied to all exposures to alpha particles emitted by radionuclides. This enhancement factor is described by a discrete probability distribution having 70% of the values at 1.0, 20% at 1.5, 7.5% at 2.0, and 2.5% at 3.0. Since the two probability distributions that apply to alpha particles have a lower bound of 1.0, truncation of the aggregate probability distribution at 1.0, based on an assumption that the biological effectiveness of alpha particles should not be less than that of high-energy gamma rays, is not needed. Acute exposures to alpha particles are not expected to be of concern for workers or the public.

Photons

Cancer risks per unit absorbed dose at low doses and low dose rates of photons are estimated using eq. (7). At energies greater than 250 keV, the RBE factor is assumed to be 1.0, without uncertainty. At energies of 30-250 keV, the RBE factor at low doses and low dose rates of the reference gamma radiation, $\overline{\text{RBE}}_{\gamma,\text{M}}$, is described by a probability distribution in which a weight of 0.25 is assigned to the value 1.0 and a weight of 0.75 is assigned to a lognormal distribution having a 95% confidence interval between 1.0 and 5.0. At energies less than 30 keV, the probability distribution of $\overline{\text{RBE}}_{\gamma,\text{M}}$ is increased by a small adjustment factor which is based on a calculation of the effective quality factor vs. energy by the ICRU (1986). This adjustment factor is described by a triangular probability distribution having a minimum of 1.0, a mode of 1.3, and a maximum of 1.6. The lower tail of the probability distribution of the RBE factor at any energy should be truncated at 1.0, based on an assumption that the biological effectiveness of low-energy photons should not be less than that of high-energy gamma rays.

Cancer risks from acute exposure to photons also are estimated using eq. (7). For acute exposure, however, the dose and dose-rate effectiveness factor, $DDREF_\gamma$, is assigned the single value 1.0 at doses above 0.2 Gy or, at lower doses, a probability distribution that approaches the probability distribution of $DDREF_\gamma$ for chronic exposure as the dose approaches zero.

Electrons

Cancer risks per unit absorbed dose at low doses and low dose rates of electrons are estimated using eq. (8). At energies greater than 60 keV, the RBE factor is assumed to be 1.0, without uncertainty. At energies of 15-60 keV, the RBE factor at low doses and low dose rates of the reference gamma radiation, $\overline{RBE}_{e,M}$, is described by a probability distribution which is the same as the probability distribution of the RBE factor for photons of energy 30-250 keV. At energies less than 15 keV, including beta particles emitted in ^3H decay and low-energy Auger electrons, the RBE factor at low doses and low dose rates is described by a lognormal probability distribution having a 95% confidence interval between 1.2 and 6.0, except Auger-emitting radionuclides that are known to be incorporated into DNA should be handled as special cases using techniques of microdosimetry. The probability distribution at the lowest energies has a geometric mean of 2.7 and a geometric standard deviation of 1.5. The lower tail of the probability distribution of the RBE factor at any energy should be truncated at 1.0, based on an assumption that the biological effectiveness of low-energy electrons should not be less than that of high-energy gamma rays.

Cancer risks from acute exposure to electrons also would be estimated using eq. (8), and the approach to estimating $DDREF_\gamma$ for acute exposure to photons described above would be used. However, acute exposure to electrons is unlikely to be important in exposures of workers and the public.

Summary Table

The probability distributions of RBE factors for the different radiation types developed in this report are summarized in Table 14. For each radiation type and energy, the probability distribution of the RBE factor and any modifying factors is described, and the 95% confidence intervals and central estimates (50^{th} percentiles) are given. For example, the probability distribution of the RBE factor for chronic exposure to neutrons of energy 10-100 keV is obtained by combining the separate probability distributions of the RBE factor for acute exposure to fission neutrons, an adjustment factor to account for the biological effectiveness of 10-100 keV neutrons compared with fission neutrons, denoted by AF_2, and an enhancement factor to account for the inverse dose-rate effect under conditions of chronic exposure, denoted by EF_n.

Table 1. Values of effective quality factor, $\overline{Q}$, and radiation weighting factor, w_R, for selected radiation types currently recommended for use in radiation protection[a]

Radiation type	Effective quality factor[b] ($\overline{Q}$)	Radiation weighting factor[c] (w_R)
Photons		
All energies		1
> 30 keV[d]	1	
Electrons		
All energies[e]		1
> 30 keV	1	
Tritium beta particles	2	
Neutrons		
Unknown energy[f]	25	
< 10 keV		5
10-100 keV		10
100 keV-2 MeV		20
2-20 MeV		10
> 20 MeV		5
Alpha particles	25	20

[a]Distinction between effective quality factor and radiation weighting factor is described in footnote 7 of main text.

[b]Values recommended by ICRU (1986) are based on calculations of quality factor vs. lineal energy in a 1-μm diameter sphere of tissue-equivalent material.

[c]Values recommended by ICRP (1991) and NCRP (1993).

[d]At photon energies less than 30 keV, calculated effective quality factor increases with decreasing energy (see Fig. 1).

[e]Auger electrons emitted in decay of radionuclides incorporated into DNA are excluded [see paragraphs A13 and B67 of ICRP (1991)].

[f]When neutron energy at location of interest in tissue is known, calculated values of $\overline{Q}$ vs. energy shown in Fig. 2 can be used.

Table 2. Summary of values of RBE_M for fission neutrons relative to high-energy gamma rays estimated by expert groups[a]

Biological response	ICRU (1986)	NCRP (1990)
Tumor induction	~3 - ~200	16-59
Life shortening	15-45	10-46
Transformation	35-70	3-80[b]
Cytogenetic studies[c]	40-50	34-53
Genetic endpoints[d]	10-45	5-70[e]

[a]Values of RBE_M apply at the low doses and low dose rates, and are obtained by extrapolation of data on dose-response for neutrons and the reference radiation at higher doses and dose rates; derived values of RBE_M generally are greater than the corresponding values of RBE at higher doses and dose rates. Only values for stochastic endpoints obtained from studies in mammalian systems are given.

[b]Value of 80 was derived from one set of experiments only.

[c]Studies on human lymphocytes in culture.

[d]Studies in mammalian systems only; range of values for genetic endpoints in plant systems estimated by NCRP (1990) is 2-100.

[e]Value of 70 derived from data on specific locus mutations in mice is not necessarily an RBE_M.

Table 3. Values of RBE_H and RBE_M of fission neutrons for life-shortening in various strains of mice derived from analysis of selected studies by Edwards (1999)[a]

Strain and Reference	RBE_H			RBE_M		
	LL[b]	Mean	UL[b]	LL[b]	Mean	UL[b]
RF/Un, Upton et al. (1967)[c]						
Female	2.5	3.5	4.5	2 5	3.5 15	4.5 55
RFM, Storer et al. (1979)						
Female	2.1	2.4	2.7	6.7	7.5	8.3
BALB/c, Storer and Ullrich (1983)						
Female	3.5	4.5	5.5	12	15	18
B6CF1, Carnes et al. (1989)						
Male	7	8	9	35	50	65
Female	8.5	9.5	10.5	34	45	56

[a]See Table 3 of Edwards (1999). RBE_H is RBE at high acute doses of reference high-energy gamma radiation, and RBE_M is RBE at low doses and low dose rates obtained by extrapolation of data on dose-response for neutrons and the reference radiation. Life-shortening in these studies was due mainly to induction of cancers. When two sets of values are given, they represent alternative interpretations that are consistent with the data.

[b]LL and UL are the lower and upper 68% confidence limits, respectively, corresponding to one standard error.

[c]Results from a study using *X* rays as the reference radiation are omitted.

Table 4. Values of RBE_H and RBE_M of fission neutrons for induction of specific cancers in various strains of mice derived from analysis of selected studies by Edwards (1999)[a]

		RBE_H			RBE_M		
Strain	Cancer	LL[b]	Mean	UL[b]	LL[b]	Mean	UL[b]
RF/Un	Myeloid leukemia	1.7	2.8	4.7	9	19	38
	Lymphoma	2.2	2.9	3.7	2.7	4.7	5.6
RFM							
Male	Myeloid leukemia	2.2	2.8	3.8	—	—	—
Female	Thymic leukemia	3.3	4.1	5.1	12	29	64
	Harderian gland tumor	7	9	11	22	33	47
	Pituitary tumor	5	7	10	17	120	∞
BALB/c							
Female	Lung adenocarcinoma	5.5	7.5	10	12	20	30
	Mammary tumor	2.5 6	3.5 11	5 20	18	27	41
CBA/H	Myeloid leukemia	4	7	10	14	21	36
SAS/4							
Male	Lung adenocarcinoma	3	5	9	—	—	—
Female	Lung adenocarcinoma	5	8	14	—	—	—

[a]See Table 4 of Edwards (1999). RBE_H is RBE at high acute doses of reference high-energy gamma radiation, and RBE_M is RBE at low doses and low dose rates obtained by extrapolation of data on dose-response for neutrons and the reference radiation. When two sets of values are given, they represent alternative interpretations that are consistent with the data. Analysis was based on data in Upton et al. (1970), Ullrich et al. (1976), Ullrich and Preston (1987), Ullrich et al. (1979), Ullrich (1980), Ullrich et al. (1977), Ullrich (1984), Mole and Davids (1982), Mole et al. (1983), and Coggle (1988).

[b]LL and UL are the lower and upper 68% confidence limits, respectively, corresponding to one standard error.

Table 5. Values of RBE_H and RBE_M of fission neutrons for tumor induction in B6CF1 mice derived from analysis of selected study by Edwards (1999)[a]

Tumor	Times of death (days after irradiation)	Sex	RBE_H[b]	RBE_M[b]
Lymphocytic	600-799	Male		6.6 ± 1.8
			2.0 ± 0.3	20 ± 5
			5.7 ± 0.9	12 ± 4
				36 ± 13
		Female	5.4 ± 0.6	8.4 ± 0.7
			11.4 ± 0.6	17.8 ± 1.5
	800-999	Male	2.5 ± 0.5	9.7 ± 1.5
			6.5 ± 1.1	25.2 ± 3.2
		Female	8.5 ± 3.0	8.5 ± 1.8
			17 ± 5	15.8 ± 2.6
Vascular tissue	600-799	Male	4.7 ± 0.6	13.9 ± 2.6
		Female	3.7 ± 1.0	7.2 ± 3.2
	800-999	Male	4.8 ± 1.0	13.7 ± 1.6
		Female	6.4 ± 1.4	8.9 ± 2.0
All epithelial tissue or ovary	600-799	Male	5.5 ± 1.0	23 ± 5
			11.0 ± 1.5	45 ± 7
		Female	10.5 ± 1.5	23 ± 4
	800-999	Male	6.2 ± 1.3	14.4 ± 2.9
			13.4 ± 2.2	31 ± 5
		Female	9.7 ± 1.9	19 ± 6

[a]See Table 5 of Edwards (1999). RBE_H is RBE at high acute doses of reference high-energy gamma radiation, and RBE_M is RBE at low doses and low dose rates obtained by extrapolation of data on dose-response for neutrons and the reference radiation. Analysis was based on data in Grahn et al. (1992). When two sets of values are given, they represent alternative interpretations that are consistent with the data.

[b]Uncertainties are one standard error.

Table 6. Quality factors for neutrons currently used by U.S. Nuclear Regulatory Commission and U.S. Department of Energy[a]

Neutron energy (MeV)	Mean quality factor[b]
≤0.001	2
0.01	2.5
0.1	7.5
0.5	11
1	11
2.5	9
5	8
7	7
10	6.5
14	7.5
20	8
40	7
60	5.5
100	4
≥200	3.5

[a]Values given in NRC (1991) and DOE (1993) are based on calculations and recommendations in NCRP (1971).

[b]Maximum calculated quality factors in a 30-cm diameter sphere of tissue-equivalent material.

Table 7. Values of RBE_M for alpha particles obtained from reviews and analyses of selected studies by the NCRP (1990) and Muirhead et al. (1993)[a]

Endpoint	RBE_M	Reference
Lung tumors (various species)	30 (6-40)	ICRP (1980)[b]
Bone tumors (dogs)	26	NCRP (1990)[c]
Bone tumors (mice)	25	NCRP (1990)[c]
Lung tumors (dogs)	30-60	NCRP (1990)[d]
Bone tumors (dogs)	4-6	Griffith et al. (1991)
Lung tumors (rats)	25	Hahn et al. (1991)
Lung tumors (dogs)	36	Hahn et al. (1991)[e]
Cell transformation (C3H10T½ mouse cells)	10-25	Brenner (1990)
Cell mutation (Chinese hamster cells, V79)	Up to 18	Thacker et al. (1979)
Chromosome aberrations (liver cells of Chinese hamster)	15-20	Brooks et al. (1972); Brooks (1975)
Chromosome aberrations (human lymphocytes)	5-35	Edwards et al. (1980); Purrott et al. (1980)
Germ cell mutations (chromosome fragments, chromosome translocations, dominant lethals)	22-24	Searle et al. (1976)

[a]Based on data presented in Section 7 of NCRP (1990) and Table 7.3 of Muirhead et al. (1993). RBE_M is RBE at low doses and low dose rates of reference radiation obtained by extrapolation of data on dose-response for alpha particles and reference radiation at high doses. Reference radiation in all studies was either beta particles from decay of radionuclides or high-energy gamma rays from ^{60}Co decay.

[b]Range based on analyses of dose-response at 10% and 40% lung tumor incidence for inhalation of soluble and insoluble alpha-emitting radionuclides combined; estimates based on analyses for inhalation of insoluble ^{239}Pu oxide only range from about 10 to nearly 100.

[c]Value based on re-analysis of preliminary data in Mays and Finkel (1980).

[d]Range based on preliminary results from Boecker et al. (1988) and Griffith et al. (1987); value toward upper end of range is not supported by subsequent analysis by Hahn et al. (1991), and value from Boecker et al. (1988) could be as low as 10.

[e]Result based on subsequent analysis of data in Boecker et al. (1988) and Griffith et al. (1987).

Table 8. Dose-response relationships of *X* rays and reference gamma rays for induction of dicentric chromosomes in human lymphocytes[a]

Reference	Radiation	Dose range[b] (Gy)	$\alpha \pm SE$[c] ($\times 10^{-2}$ Gy^{-1})	$\beta \pm SE$[c] ($\times 10^{-2}$ Gy^{-2})
Bauchinger (1984)	220 kVp *X* rays	0.5-4	4.0 ± 0.3	5.98 ± 0.17
	^{60}Co γ rays	0.5-4	1.1 ± 0.4	5.55 ± 0.28
Fabry et al. (1985)	250 kVp *X* rays	0.05-2	4.4 ± 1.0	6.0 ± 1.1
	^{60}Co γ rays	0.05-2	3.0 ± 0.8	4.3 ± 1.0
Lloyd et al. (1986)	250 kVp *X* rays	0.05-6	3.6 ± 0.5	6.67 ± 0.22
	^{60}Co γ rays	0.05-6	1.4 ± 0.4	7.59 ± 0.27
Littlefield et al. (1989)	220 kVp *X* rays	0.25-3.75	4.3 ± 0.8	6.6 ± 0.4
	^{60}Co γ rays	0.25-4	1.6 ± 0.7	5.7 ± 0.3
Brewen and Luippold (1971)[d]	250 kVp *X* rays	0.5-4	9.1 ± 0.2	6.0 ± 0.7
Brewen et al. (1972)[d]	^{60}Co γ rays	0.5-4	3.9 ± 1.1	8.2 ± 0.4
Lloyd et al. (1975)	250 kVp *X* rays	0.05-8	4.8 ± 0.5	6.2 ± 0.3
	^{60}Co γ rays	0.25-8	1.6 ± 0.3	5.0 ± 0.2

[a]See Tables 2.6 and 2.7 of NCRP (1990).

[b]Doses were delivered acutely or over a time period of about 10 minutes or less.

[c]α and β are coefficients of linear and quadratic terms in dose-response relationship, and SE is the standard error.

[d]Results for *X* rays and gamma rays were reported separately.

Table 9. Estimates of RBE_M for *X* rays for induction of dicentric chromosomes in human lymphocytes[a]

Reference	*X* rays	RBE_M (68% CI)[b]
Bauchinger (1984)	220 kVp	3.8 (2.5, 6.5)
Fabry et al. (1985)	250 kVp	1.5 (1.0, 2.2)
Lloyd et al. (1986)	250 kVp	2.6 (1.8, 3.8)
Littlefield et al. (1989)	220 kVp	2.8 (1.7, 5.1)
Brewen and Luippold (1971); Brewen et al. (1972)	250 kVp	2.3 (1.8, 3.3)
Lloyd et al. (1975)	250 kVp	3.0 (2.4, 3.8)

[a]RBE_M is RBE at low doses obtained by extrapolation of linear-quadratic dose-response relationships for *X* rays and reference ^{60}Co gamma rays.

[b]First entry is point estimate calculated by NCRP (1990) as α_X/α_γ, where α_X and α_γ are central estimates of coefficient of linear term in dose-response relationship for *X* rays and gamma rays, respectively, given in Table 8. Second entry in parentheses is 68% confidence interval based on standard errors in α coefficients given in Table 8 and calculated as described in text.

Table 10. Estimates of RBE of tritium beta particles for carcinogenesis endpoints[a]

Effect	Radiation and conditions	RBE	Reference
Mammary tumors in S-D rats	HTO and chronic *X* rays	1.2 ± 0.3	Gragtmans et al. (1984)
Leukemia in CBA/H mice	HTO and chronic *X* rays	1.2 ± 0.3	Myers and Johnson (1991)
Tumors in C57B1/6N × C3H/He mice	HTO and acute gamma rays	~1[b]	Yokoro et al. (1989)
Transformation in hamster cells *in vitro*	HTO and acute *X* rays	~1	Suzuki et al. (1989)
Transformation in mouse cells *in vitro*	HTO and acute *X* rays	1-2	Little (1986)
Transformation in 10T½ cells	HTO and subacute gamma rays	1.4-1.8	Yamaguchi et al. (1985)

[a]See Table 1 of Straume and Carsten (1993).

[b]Authors did not provide a value of RBE but state that HTO was not very different from gamma rays.

Table 11. Estimates of RBE of tritium beta particles for genetic endpoints[a]

Effect	Radiation and conditions	RBE	Reference
6-Thioguanine resistance in mouse cells *in vitro*	HTO and chronic gamma rays	2.9	Ueno et al. (1989)
6-Thioguanine resistance in mouse cells *in vitro*	^{3}H-amino acid and chronic gamma rays	2.6	Ueno et al. (1989)
6-Thioguanine resistance in mouse cells *in vitro*	Tritiated thymidine (^{3}H-Tdr)[b] and chronic gamma rays	5.9	Ueno et al. (1989)
6-Thioguanine resistance in mouse cells *in vitro*	HTO and gamma rays at 10^{-5} mutant frequency		Nakamura et al. (1985)
	acute	1.5	
	chronic	2.4	
Chromosome aberrations in human sperm *in vitro*	HTO and chronic *X* rays	3	Kamiguchi et al. (1990)
Chromosome aberrations in fish lymphocytes *in vitro*	HTO and chronic gamma rays	1.9	Suyama and Etoh (1985)
Chromosome aberrations in mouse zygotes	HTO and chronic gamma rays	1.8	Matsuda et al. (1985)
Chromosome aberrations in CBA/H mice			Chopra and Heddle (1988)
lymphocytes	HTO and *X* rays	1.1	
spermatogonia	HTO and *X* rays	1.2	
Micronuclei in mammalian cells	HTO and chronic gamma rays	2.0 2.7	Ueno et al. (1982) Kashima et al. (1985)
Mutations in *Drosophila* spermatozoa	HTO and gamma rays	2.7	Byrne and Lee (1989)
Mutations in mice *in vivo*	HTO and chronic gamma rays	2.7	Nomura and Yamamoto (1989)

Table is continued on following page.

Table 11. (continued)

Effect	Radiation and conditions	RBE	Reference
Dominant lethals in male mice	HTO and chronic gamma rays	2.5	Searle (1984)
		1-2	Carsten and Commerford (1976)
Dominant lethals in female mice	HTO and chronic gamma rays	2.5	Xiang-yan et al. (1986)
Specific locus mutations in male mice	HTO and chronic gamma rays	2.0	UNSCEAR (1982)
Dominant lethals in male mice	HTO and chronic gamma rays	2.5	Searle (1984)
		1-2	Carsten and Commerford (1976)

[a]See Table 2 of Straume and Carsten (1993).
[b]Use of methyl-^{3}H-Tdr resulted in identical RBEs.

Table 12. Estimates of RBE for ^{3}H beta particles for chromosome aberrations in human lymphocytes[a]

Radiation and conditions	RBE	Reference
HTO and acute *X* rays	1.9 ± 0.7	Bocian et al. (1977), as refit by Prosser et al. (1983)
HTO and subacute gamma rays	1.49 ± 0.21	Morimoto et al. (1989)
HTO and acute *X* rays	1.13 ± 0.18	Prosser et al. (1983)
HTO and acute gamma rays	3.4 ± 0.6	Prosser et al. (1983) and Lloyd et al. (1975)
HTO and subacute *X* rays	2.6	Vulpis (1984)
HTO and low dose *X* rays	2.0	Estimated from Prosser et al. (1983) and Lloyd et al. (1988)

[a]See Table 3 of Straume and Carsten (1993).

Table 13. Estimates of RBE for ^{3}H beta particles for developmental and related effects[a]

Effect	Radiation and conditions	RBE	Reference
Mouse embryo, two-cell to blastocyte *in vitro*	HTO and chronic gamma rays	1.7	Yamada et al. (1982)
Teratogenic effects in rat embryos	HTO and chronic gamma rays	2.6	Satow et al. (1989)
Cell killing *in vitro*	HTO and chronic gamma rays	1.3	Ueno et al. (1989)
	^{3}H-amino acids and chronic gamma rays	1.7	
	Tritiated thymidine (^{3}H-Tdr)[b] and chronic gamma rays	3.5	

[a]See Table 4 of Straume and Carsten (1993).
[b]Use of methyl-^{3}H-Tdr resulted in identical RBEs.

Table 14. Summary of probability distributions of RBE factors to be used in estimating probability of causation of cancers from exposure to various radiation types.

Exposure information			Probability distribution of RBE factor		
			95% confidence interval[a]		
Radiation type	**Exposure**	**Description**	**2.5th**	**50th**	**97.5th**
RBE factors to be used with risks per unit dose at high doses and high dose rates of gamma radiation that are adjusted to low doses and dose rates by use of $DDREF_\gamma$					
Photons	Any[b]				
E > 250 keV		Single-valued	—	1.0	—
E = 30-250 keV		Hybrid ($\overline{RBE}_{\gamma,M}$)[c]	1.0	1.9	4.7
E < 30 keV		$\overline{RBE}_{\gamma,M} \times AF_\gamma$	1.1	2.4	6.1
Electrons	Any[b]				
E > 60 keV		Single-valued	—	1.0	—
E = 15-60 keV		Same as 30-250 keV photons	1.0	1.9	4.7
E < 15 keV[d]		Lognormal	1.2	2.7	6.0
Neutrons		Not applicable			
Alpha particles[e]	Chronic[f]	Stepwise-uniform[g] $\times EF_\alpha$	3.0	26	86
RBE factors to be used with risks per unit dose at high doses and high dose rates of gamma radiation, without adjustment to low doses and dose rates by use of $DDREF_\gamma$					
Electrons		Not applicable			
Photons		Not applicable			
Neutrons					
E = 0.1-2 MeV[h]	Acute	Lognormal ($\overline{RBE}_{n,H}$)	1.5	6.7	30
	Chronic	$\overline{RBE}_{n,H} \times EF_n$	1.8	8.9	47
E = 10-100 keV;	Acute	$\overline{RBE}_{n,H}/AF_2$	0.6	3.4	17
E = 2-20 MeV	Chronic	$\overline{RBE}_{n,H} \times EF_n/AF_2$	0.8	4.4	27
E < 10 keV;	Acute	$\overline{RBE}_{n,H}/AF_4$	0.3	1.7	8.7
E > 20 MeV	Chronic	$\overline{RBE}_{n,H} \times EF_n/AF_4$	0.4	2.2	13
Alpha particles		Not applicable			

See following page for footnotes and legend.

Footnotes for Table 14

[a]Lower tails of probability distributions of RBE factors for photons, electrons, and neutrons should be truncated at 1.0; probability distribution for alpha particles has lower bound of 1.0.

[b]For acute exposure to photons or electrons, estimated risks are adjusted by dose and dose-rate effectiveness factor, $DDREF_\gamma$, that depends on the dose received. For acute doses greater than 0.2 Gy, $DDREF_\gamma = 1.0$. For acute doses less than 0.2 Gy, a $DDREF_\gamma$ that can exceed 1.0 is applied; the distribution of possible values approaches $DDREF_\gamma$ for chronic exposure as the dose approaches zero.

[c]Probability distribution assigns weight of 0.25 to value of 1.0 and weight of 0.75 to lognormal distribution having 95% confidence limit between 1.0 and 5.0.

[d]Energy range includes beta particles emitted in decay of ^3H and low-energy Auger electrons; RBE factor does not apply to Auger-emitting radionuclides that are known to be incorporated into DNA.

[e]RBE factor is not applied to inhalation of radon and its short-lived decay products.

[f]Acute exposures to alpha particles emitted by radionuclides generally should not occur.

[g]Probability distribution has 15% of values in range of 1.0-10, 25% in range of 10-20, 30% in range of 20-30, 20% in range of 30-40, 7.5% in range of 40-60, and 2.5% in range of 60-100.

[h]RBE factors for this energy range apply to fission neutrons.

Legend for Table 14

$\overline{RBE}_M$	RBE factor at low doses and low dose rates of reference high-energy gamma radiation.
$\overline{RBE}_H$	RBE factor at high acute doses of reference high-energy gamma radiation; probability distribution is applied at any dose and dose rate of neutrons.
AF_γ	Increase in biological effectiveness, relative to photons of energy 30-250 keV, for photons of energy <30 keV; probability distribution is triangular (minimum of 1.0, mode of 1.3, and maximum of 1.6).
EF_α	Factor representing inverse dose-rate effect for chronic exposure to alpha particles; probability distribution is discrete (70% at 1.0, 20% at 1.5, 7.5% at 2.0, and 2.5% at 3.0).
EF_n	Factor representing inverse dose-rate effect for chronic exposure to neutrons; probability distribution is discrete (50% at 1.0, 30% at 1.5, 15% at 2.0, and 5% at 3.0).
AF_2	Reduction in biological effectiveness, relative to fission neutrons, for neutrons of energy 10-100 keV or 2-20 MeV; probability distribution is lognormal (95% confidence interval between 1.0 and 4.0).
AF_4	Reduction in biological effectiveness, relative to fission neutrons, for neutrons of energy <10 keV or >20 MeV; probability distribution is lognormal (95% confidence interval between 2.0 and 8.0).
$DDREF_\gamma$	Dose and dose-rate effectiveness factor used to adjust risk estimates that apply at high doses and high dose rates of high-energy gamma radiation to exposures at low doses and low dose rates of low-LET radiations.

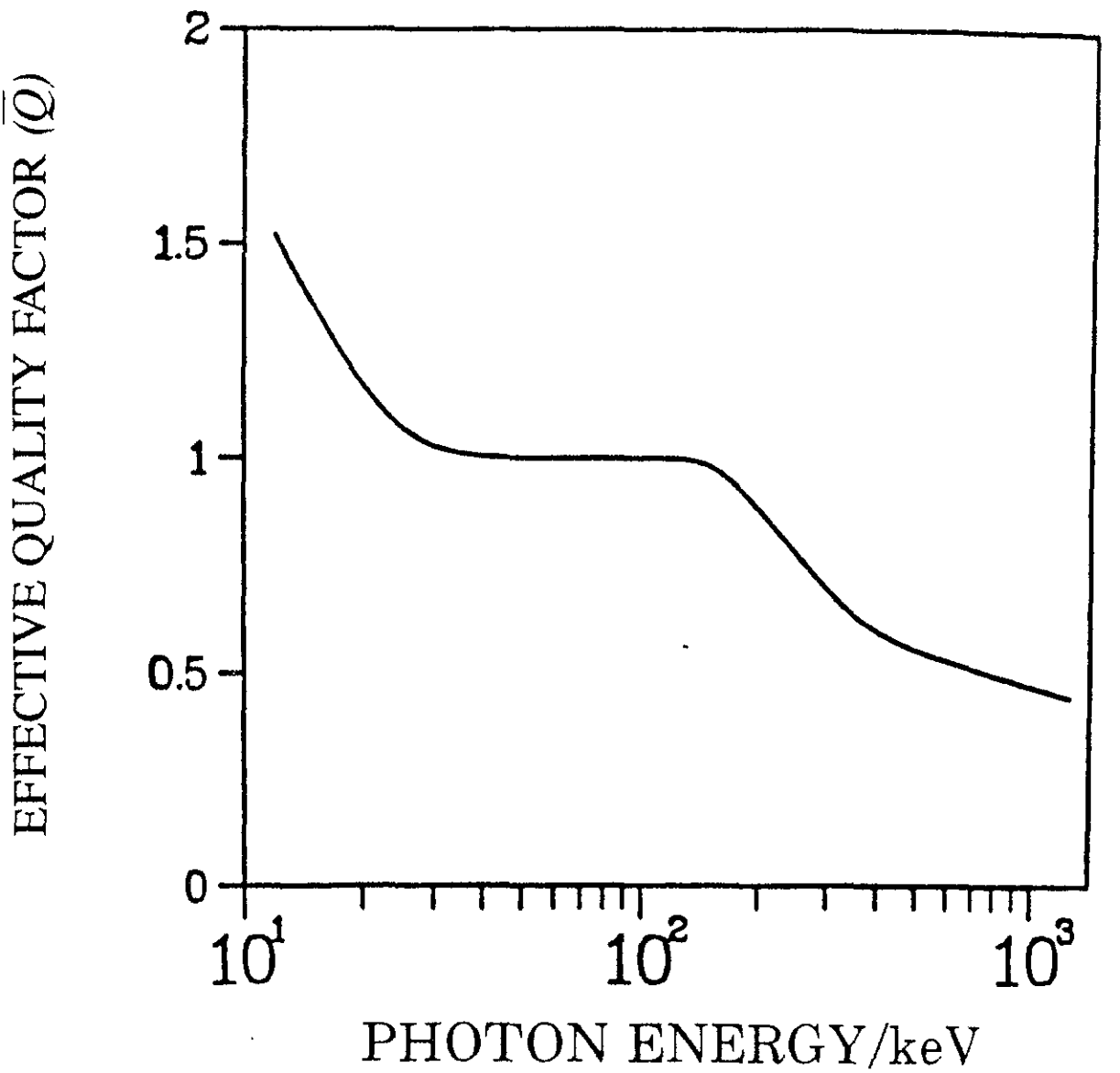

Fig. 1. Calculated values of effective quality factor, $\overline{Q}$, vs. photon energy under conditions of charged-particle equilibrium given in Fig. 3 of ICRU (1986). Quality factor is normalized to unity at energies of orthovoltage *X* rays often used in radiobiological studies; value for gamma rays emitted in ^{60}Co decay is at right end of curve.

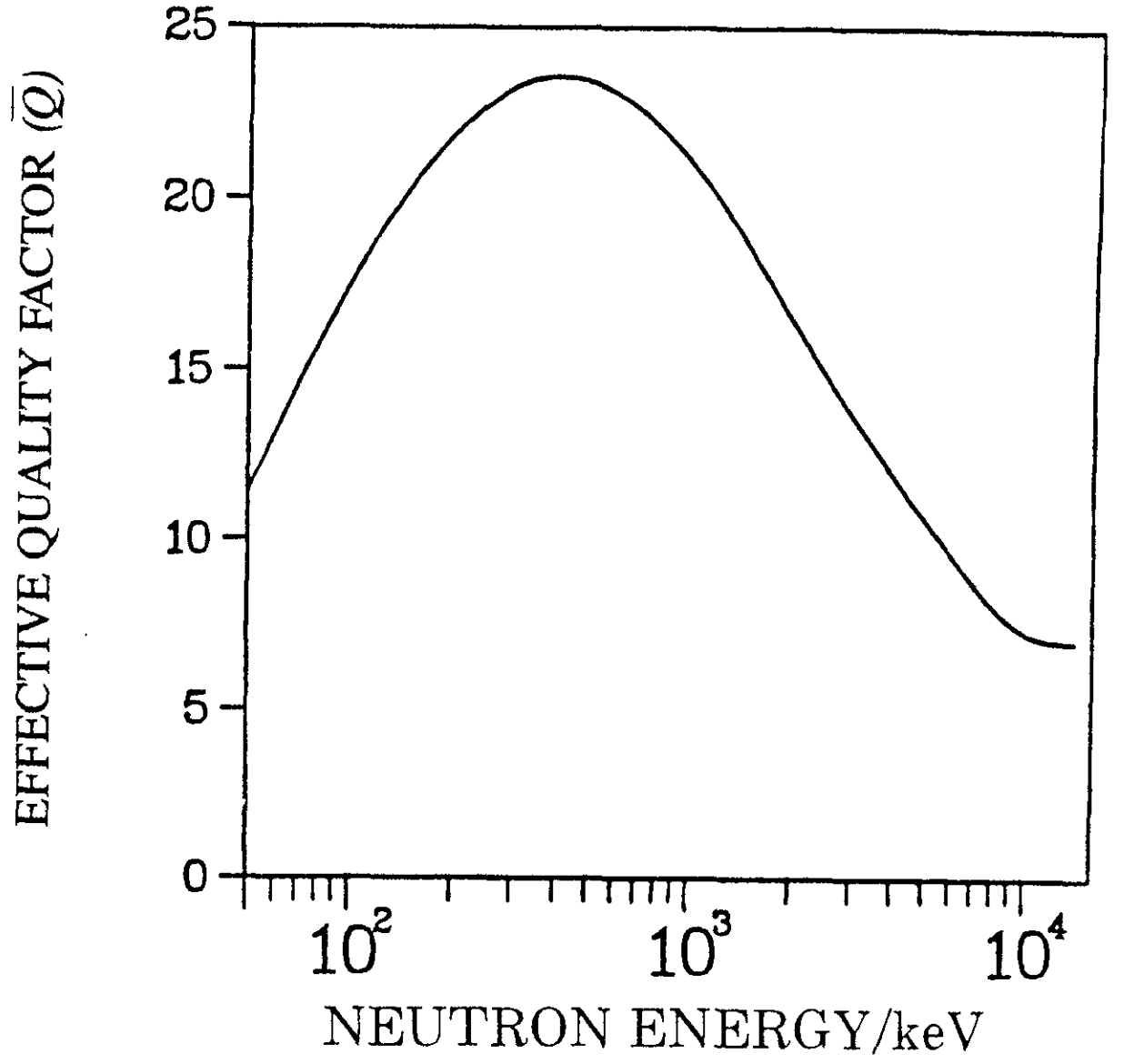

Fig. 2. Calculated values of effective quality factor, $\overline{Q}$, vs. neutron energy under conditions of charged-particle equilibrium given in Fig. 4 of ICRU (1986).

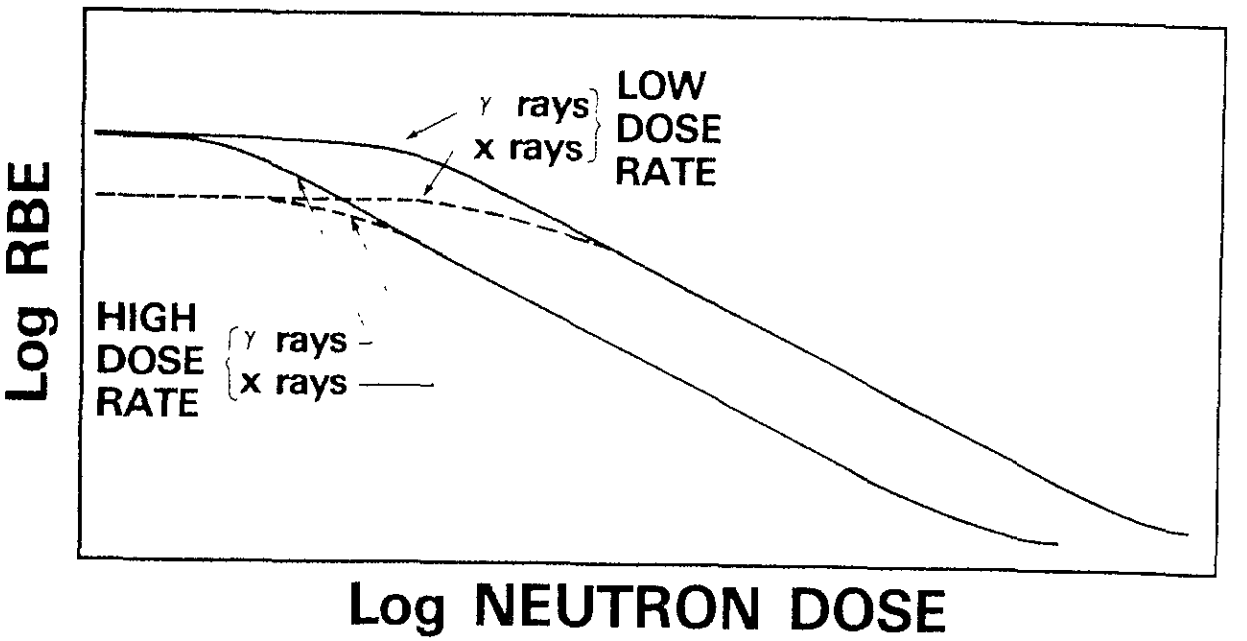

Fig. 3. Schematic representation of increase in RBE for fission neutrons with decreasing dose given in Fig. C-2 of ICRU (1986). Maximum values at low doses are values of RBE_M.

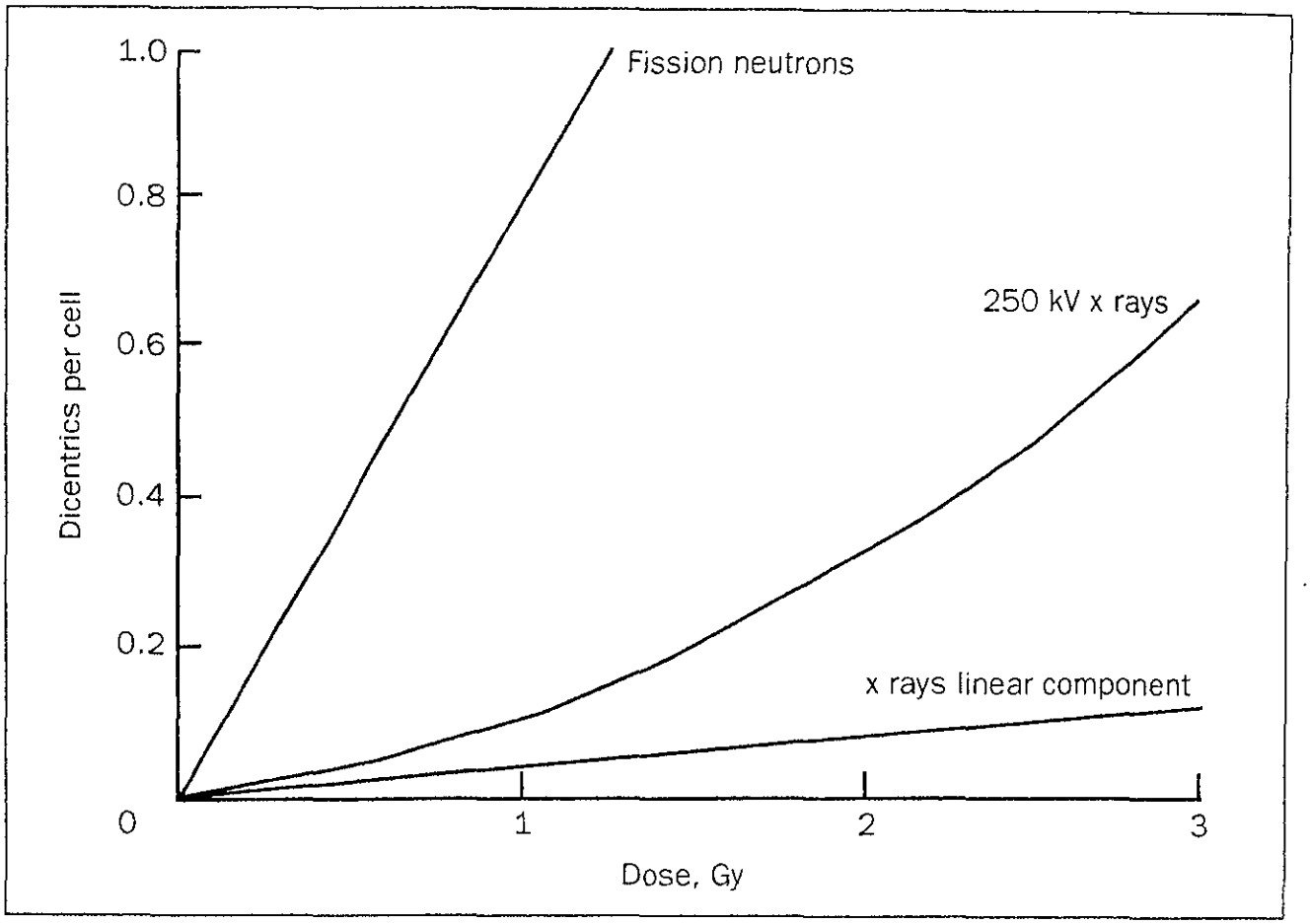

Fig. 4. Representation of linear and linear-quadratic dose-response relationships for fission neutrons and *X* rays, respectively, in studies of induction of dicentric chromosomes in human lymphocytes given in Fig. 1 of Edwards (1997). Separation of two curves at different levels of response illustrates dependence of neutron RBE on dose, as shown in Fig. 3; RBE at low doses and low dose rates, RBE_M, is determined by separation of neutron curve and linear component of *X* ray curve.

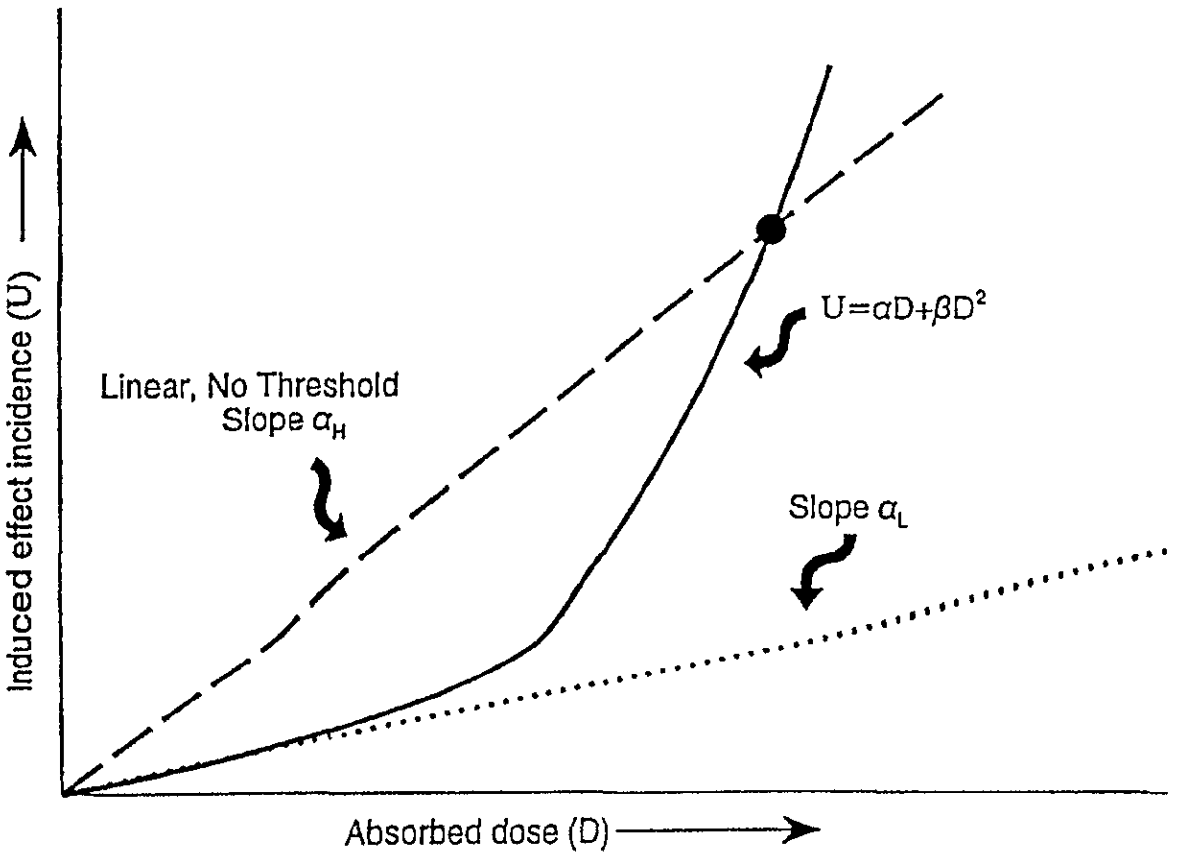

Fig. 5. Representation of linear-quadratic dose-response relationship for low-LET radiations given in Fig. 2 of CIRRPC (1995). Dose and dose-rate effectiveness factor (DDREF) is ratio of linear extrapolation at high doses, α_H, to slope of dose-response curve at low doses, α_L, and, thus, is a function of dose given by $1 + (\beta/\alpha)D$.

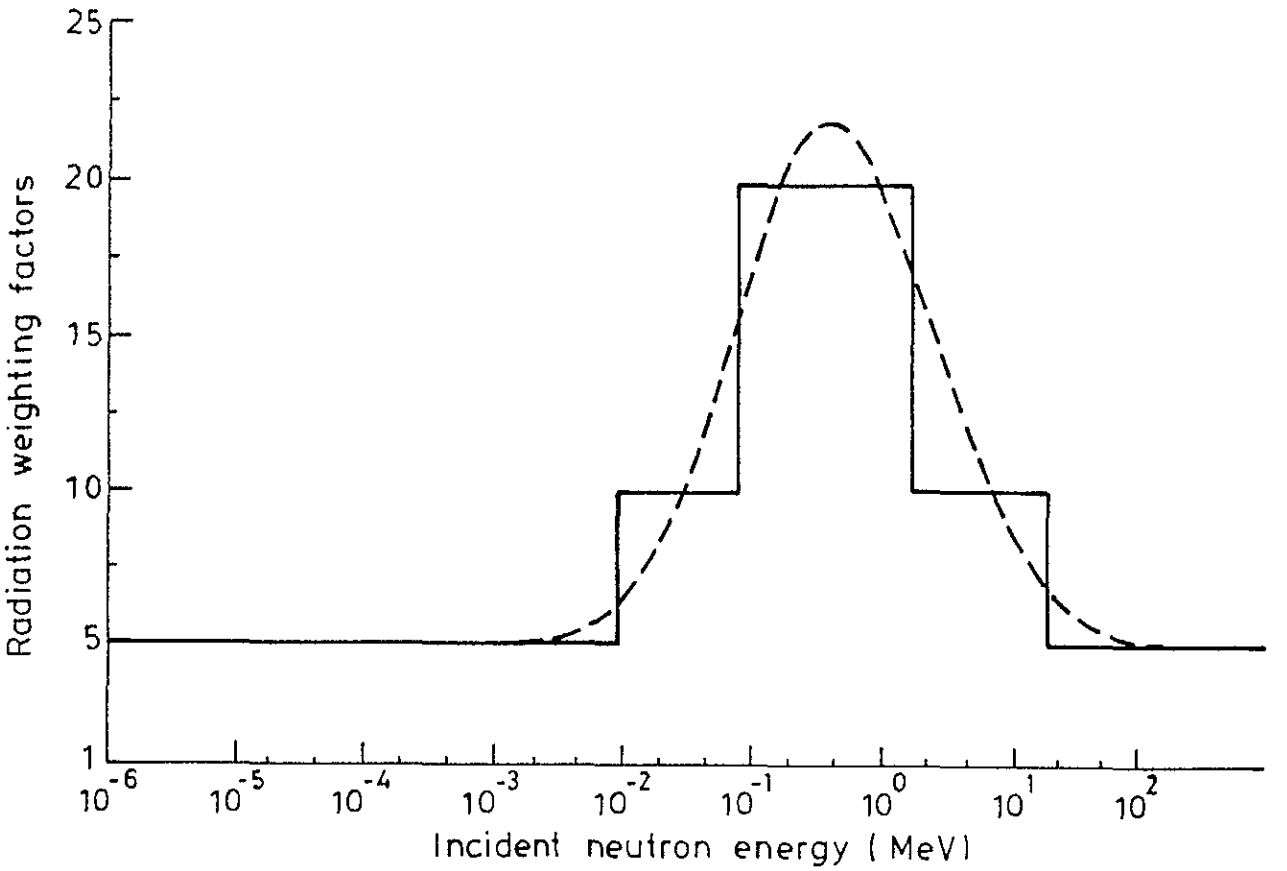

Fig. 6. Radiation weighting factor, w_R, vs. neutron energy currently recommended by ICRP (1991) and NCRP (1993) and given in Fig. A.1 of ICRP (1991). Dashed curve is an approximate given by eq. (4).

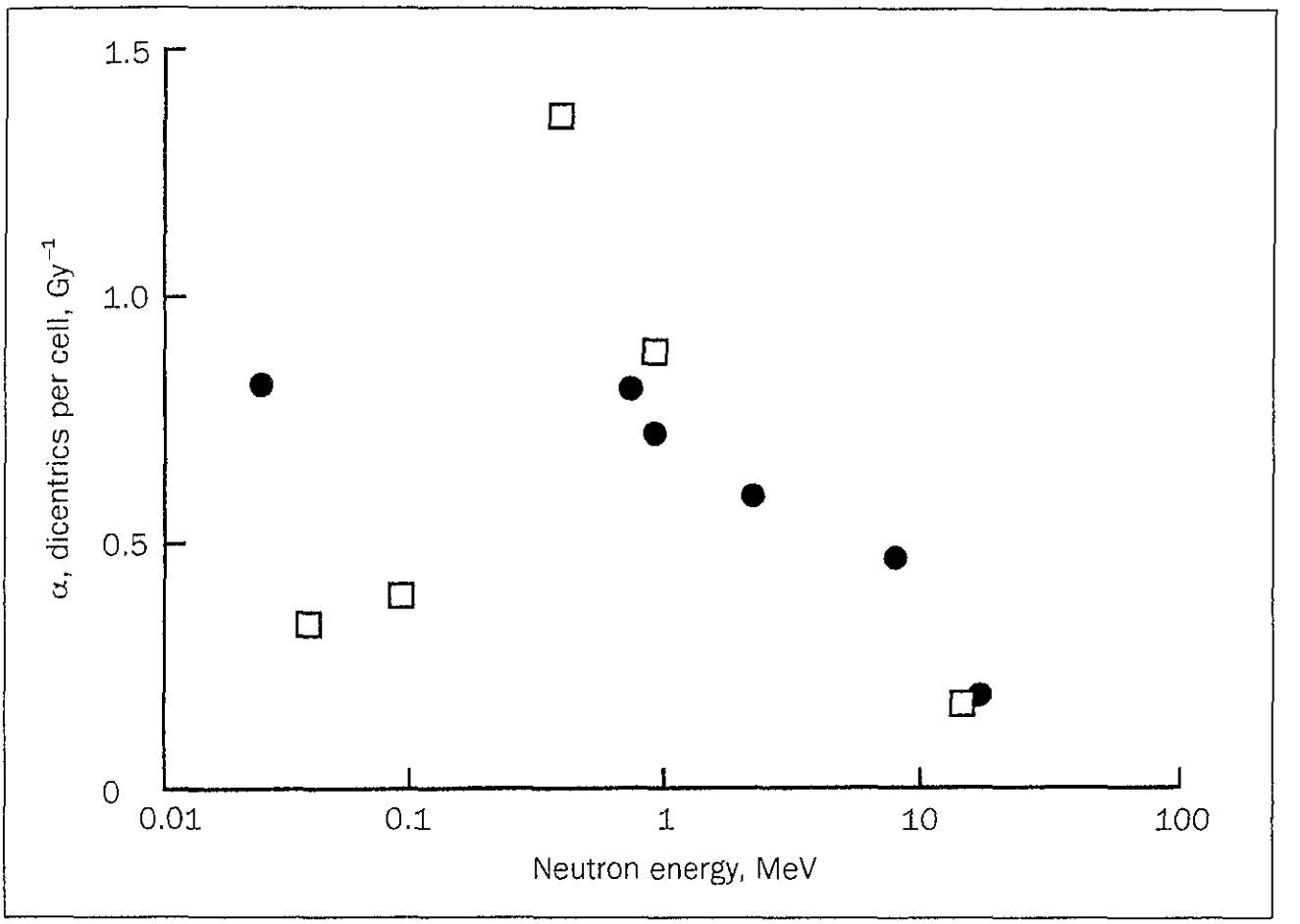

Fig. 7. Variation of RBE_M with neutron energy for induction of dicentric chromosomes in human lymphocytes shown in Fig. 6 of Edwards (1997; 1999). Solid circles are data of Edwards et al. (1985; 1990), and open squares are data of Sevan'kaev et al. (1979).

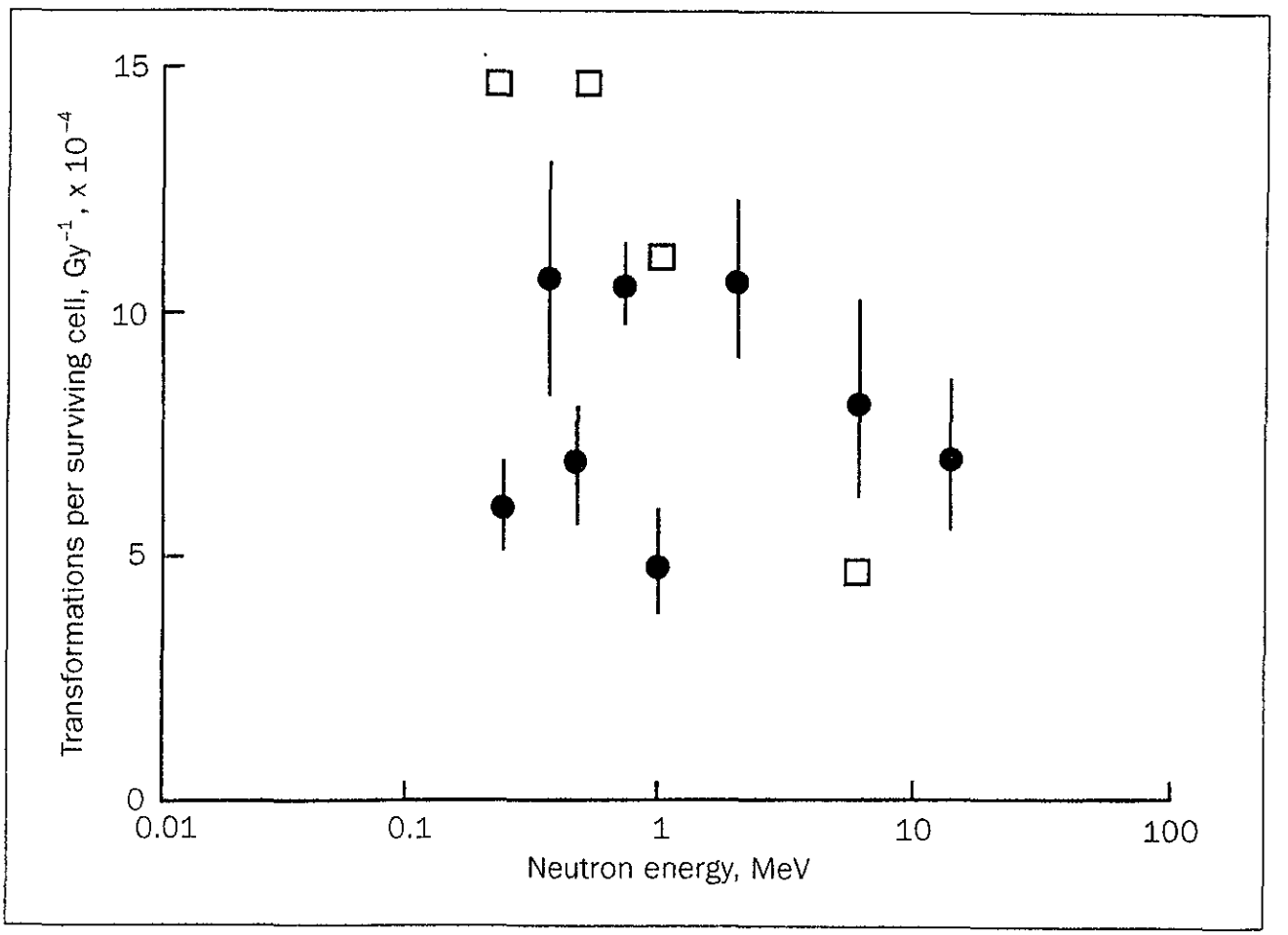

Fig. 8. Variation of RBE_M with neutron energy for transformation of C3H10T½ mouse cells shown in Fig. 7 of Edwards (1997). Solid circles are data of Miller et al. (1989), and open squares are data of Coppola (1993); error bars represent one standard error.

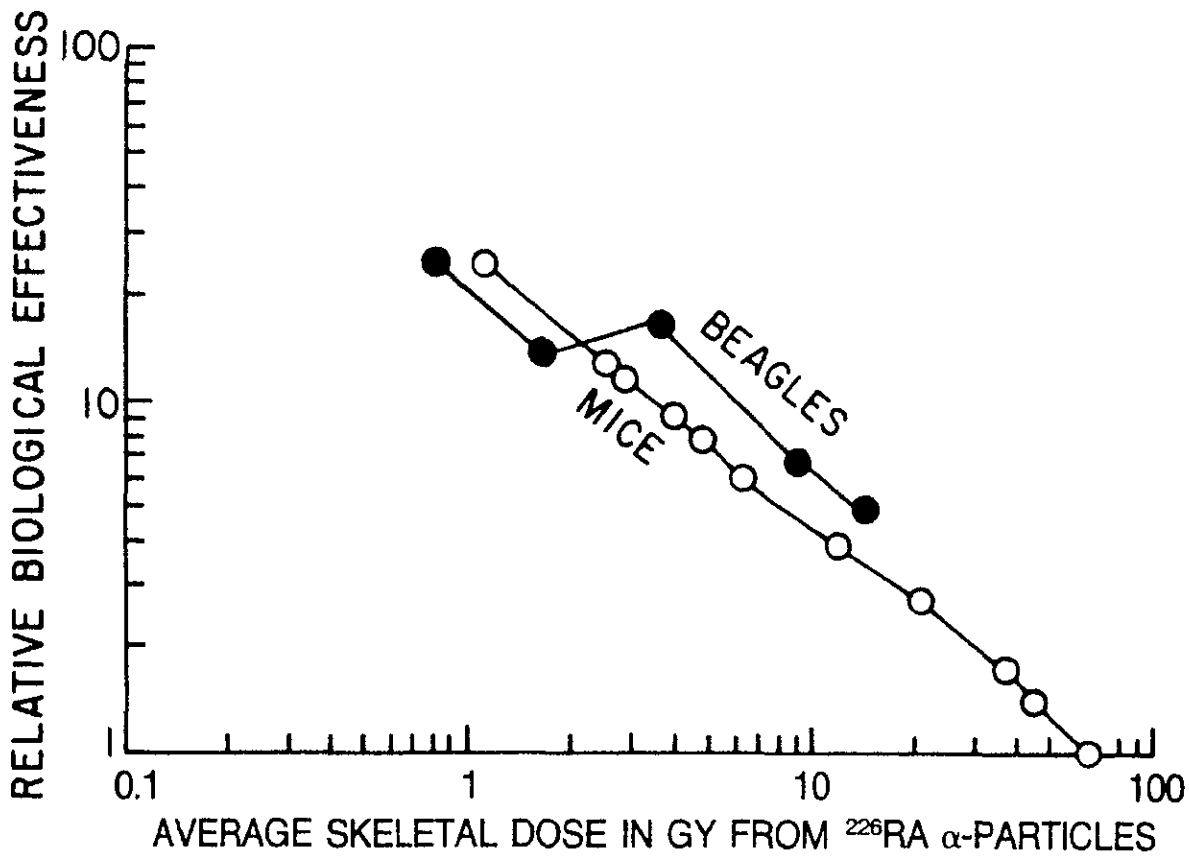

Fig. 9. Biological effectiveness of alpha particles emitted by ^{226}Ra and its decay products, relative to beta particles emitted by ^{90}Sr and ^{90}Y, for induction of bone tumors in mammals given in Fig. 7.3 of NCRP (1990); curves show pronounced dependence of RBE on dose.

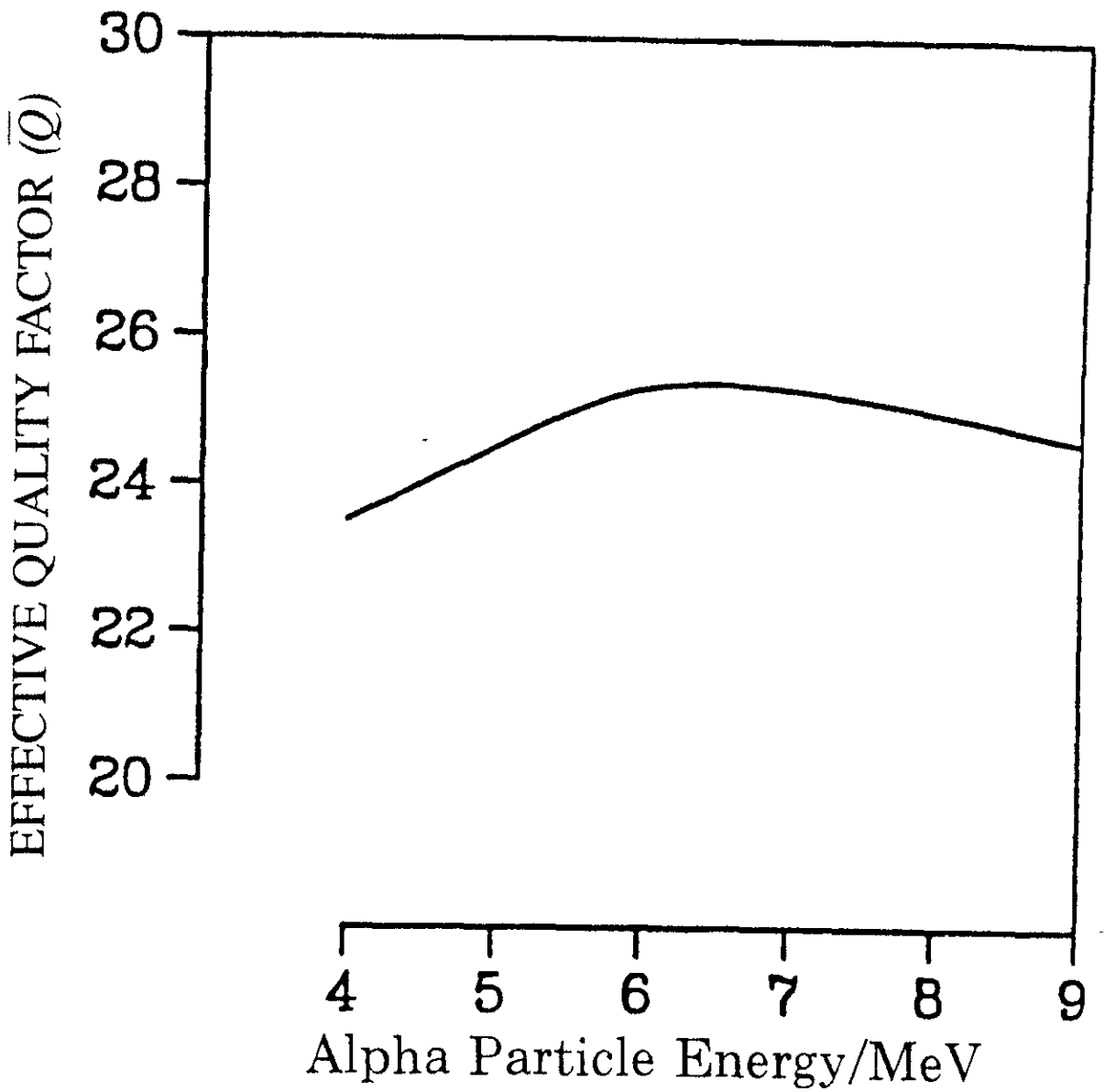

Fig. 10. Calculated values of effective quality factor, $\overline{Q}$, vs. alpha particle energy given in Fig. 5 of ICRU (1986). Values apply to entire range of alpha particles of given initial energy.

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